Smart Systems for Healthcare and Wellness

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Smart Systems for Healthcare and Wellness

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Abstract:

The cost of health care is increasing tremendously in Europe. If no action is taken, healthcare might become unaffordable for all its citizens. To curb the exploding costs in healthcare, actions on various levels need to be taken: economical, organizational and technological. One of the measures to be taken is to prevent people becoming ill. Curing people is much more expensive than prevention. This can be reached by promoting personalized and preventive healthcare. People should be empowered to monitor their own health, be given continuous feedback to improve their health and lifestyle, or just simply by being able to enhance their quality of life. This needs the right set of tools, and thus calls for development of technology, that is easy to use, but still accurate and in case of wearable sensors, it should be comfortable and unobtrusive. And last but not least, they need to be affordable.

Micro and Nanotechnology can play a key role here. Over the last 60 years, semiconductor technology has progressed tremendously. Following Moore's law, huge computation power has become available into handheld devices, sensors have shrunk in size, and wireless communication has penetrated into the consumer market, to name only a few developments. The next step is the migration into wearable devices. Already many products are appearing on the market, but with limited functionality and unfit for long term continuous monitoring. More research is needed to obtain that goal. This report will focus on the technology challenges that still lie ahead, and discuss possible solutions.

In this report various technologies are reviewed with the following keywords in mind: prevention (including the promotion of healthy lifestyle through fitness and stress monitoring), diagnostic, therapy and therapy monitoring as well as decentralization from hospital to home maintenance. Three large applications are targeted: Devices for the healthy, devices to cure, and devices to aid the chronically ill ("stay fit", "get well", "a better live"). They have to operate unobtrusive, need full autonomy and are either wearable or implantable. Small devices (cm to mm size), with a typical power budget between several μW and a few mW are envisaged.

Chapter 1 Introduction

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1.1 The increase of healthcare cost

The healthcare system in the western world are facing daunting challenges. Above all, the cost of health care is increasing tremendously (see Figure 1.1). This is especially the case in the US, where the healthcare costs in the last 40 years has doubled to a value of $7.290/Capita (2007 [1]), more than double the value of countries like Germany, United Kingdom and the Netherlands. At the same time, millions of people in the US do not have access to health care at all.

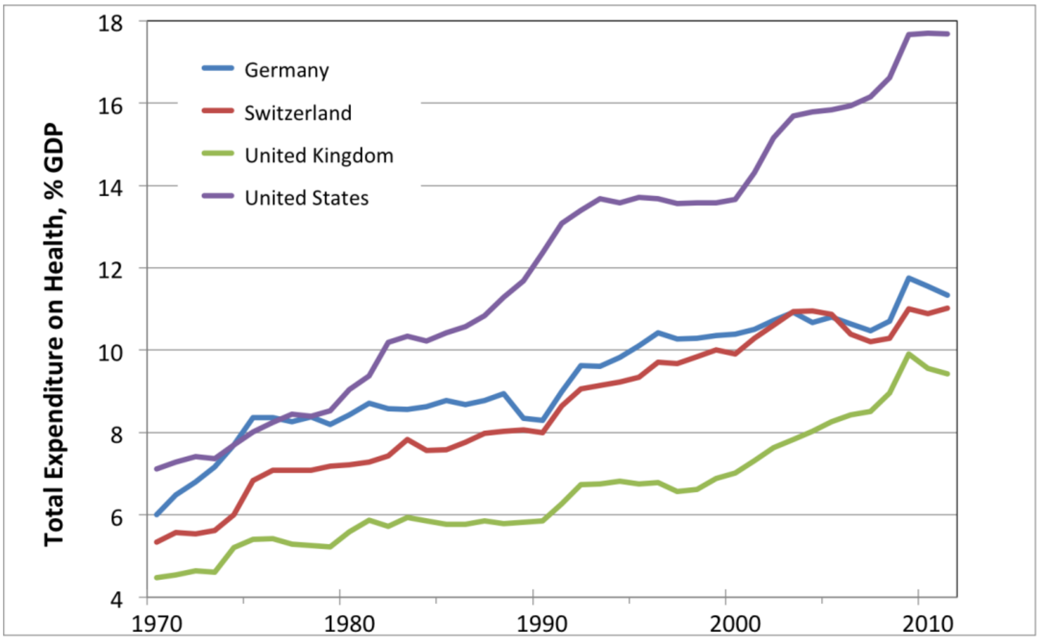

Figure 1.1 : Healthcare expenditure increase of a few selected countries (OECD data [1])

Many times, demographic changes are blamed for the rise in costs. As can be seen in Figure 1.2, the percentage of aged 65+ years has steadily increased over the last 25 years and are even to accelerate in the future, reaching values between 20 to 30%. However, data in Japan suggest that there is no direct relationship. However, as is pointed out in [2], "With the longest life expectancy in the world—and one that European countries are not expected to reach for over two decades—it spends only 8.5% of its GDP on healthcare, less than the OECD average". A frequently cited 2007 study of healthcare spending across OECD countries between 1970 and 2002 found that, outside of the United States, on average ageing drove a rise in health spending of 0.5% per year, and other factors accounted for 3.2% [3]. Also, the steady progress is biomedicine and science has increased the survival from acute trauma, but this is associated with an increase in the number of individuals with severe disabilities[4].

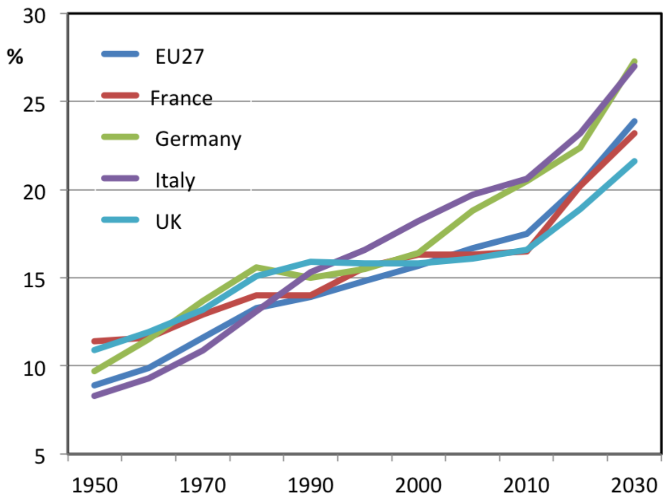

Figure 1.2: Percentage aged 65+ years for a few European countries (source: UN)

The majority of the disease load are the chronic diseases. According to the OECD, between 10% and 20% of West Europeans over 65 require some form of long-term care. Integrating this provision with health systems will become more important as the number over that age increases. Originally designed for acute, episodic care rather than ongoing treatment of chronic conditions, health systems are not good at providing the ongoing, co-ordinated care required by the latter [2].

A second important element will have to be the focus on prevention. Candace Imison, deputy director of policy at The King's Fund, a British healthcare think tank, cites as a major challenge "behaviours within the population that are driving health needs: obesity, alcohol abuse, smoking, lack of exercise"[2]. In Table 1.1 some numbers are given for a few western countries

Table 1.1: Overweight/Obese, Adult smokers and alcohol consumption for a few western countries (Sources: OECD; World Health Organisation (WHO))

	Overweight or obese people (%)	Adult smokers (%)	Alcohol consumption per head (litres)
Denmark	45	20	13.4
France	37	26	13.7
Germany	50	22	12.8
Netherlands	46	28	10.1
UK	61	22	13.4

1.2 Technology driven Decrease cost and promote prevention

It is now recognized that the monitoring and prevention of diseases and follow-up of patients are two key components for improving the *quality of life*. The improvement in quality of life and the reduction of hospitalization bring associated cost savings at both the individual and societal levels. On the other hand similar technologies can be used for as personal trainers for wellbeing of active people. Smart systems for health and wellbeing are specially designed to simultaneously measure many physical and physiological parameters. Captured data can be analysed in real time to provide the physiological status of the person wearing the device. Such body parameters are useful for recording the physiological status of healthy people as well as that of people with a chronic disease or frailty.

In smart systems dedicated to healthcare and wellness applications the sensors collect physical, chemical and biochemical data to enable interpretation and monitoring of a person's physiological status, in relation to the actual environmental and social context. To afford a complex multi-parametric real-time sensing based on several types of sensors in portable smart systems, the power consumption per sensor element becomes a figure of merit as important as the other requirements (sensitivity, selectivity, robustness, reliability, integration on advanced silicon platform and/or flexible substrates). The power figure should include the power required by readout electronics, signal conditioning and AD conversion, but usually exclude digital signal processing such as linearization, pattern recognition and sensor fusion.

Micro and Nanotechnology can play a key role here. Over the last 60 years, technology has progressed tremendously. Following Moore's law, huge computation power has become available into handheld devices, sensors have shrunk in size, and wireless communication has penetrated into the consumer market, to name only a few developments. A schematic is shown in Figure 1.3, with sensors all over and sometimes inside the body, enabling to monitor people (e.g. 24/7) or to assist them in conducting activities that help in the prevention of diseases (e.g. fitness). These devices enable to monitor several physiological parameters, like ECG, EEG, Blood pressure.

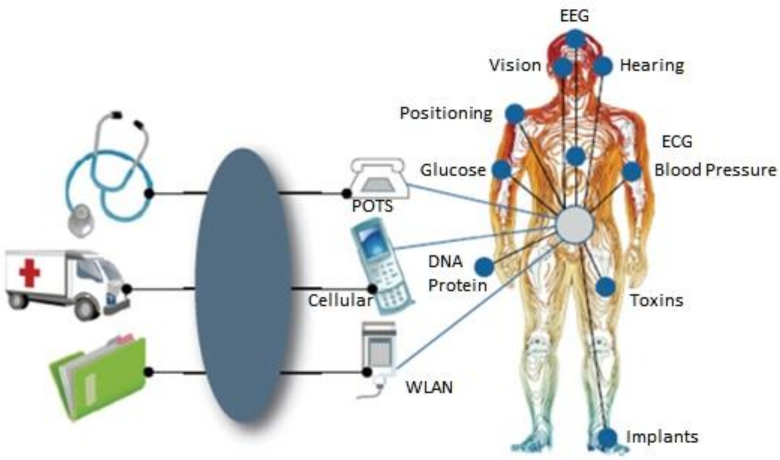

Figure 1.3: Basic schematic of the Body Sensor network. On-body or implantable sensors measure parameters, and send these to the outside world through a network connection.

1.3 Scope of the report: Body Area Network

In many cases the embodiments of smart systems for health care will be quasi-invisible, self-powered body area networks or, if appropriate, implantable devices, monitoring vital health signals and offering the necessary information for taking appropriate actions to preserve human health. They should acquire a well-defined view of the state of a person's health by using a real-time, ultra-low-power, multi-parametric combination of non-intrusive, bio-signal sensors (ECG, accelerometers, gyroscopes, pulse oximetry, etc.) to allow for early warning and thus enhancement of the quality of life. They can employ future technologies such as electronic skin or wearable self-powered networks of sensors with wireless interfaces communicating at a few meters. To benefit from already existing mobile communication technologies, such systems should be compatible, from the communication point of view, with existing gateways (such as mobile phones) to serve as smart parts of a future vision of the *internet of things [5]*. schematically show in Figure 1.4 such possible embodiments of smart systems as patchable and/or wearable sensors with communication interfaces and their own sources of energy, energy storage and power management (integrated in smart garments, smart watches, etc.).

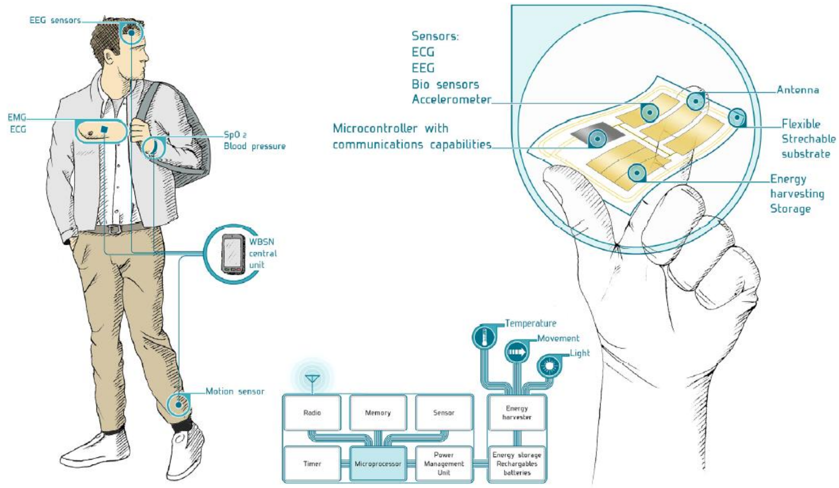

Figure 1.4: Embodiment scenario of a ***Wearable Smart System*** *for multi-parameter physical and physiological monitoring in patchable and smart clothing exploiting sensors on flexible substrates or in/on textile fibers (source: GA FET Flagship proposal [6]). The categories sensors cited in this figure can be extended, depending on the particular monitoring applications. The mobile phone can be used as the main interfaces but other alternative interfaces can be smart surfaces with tunable optical properties.*

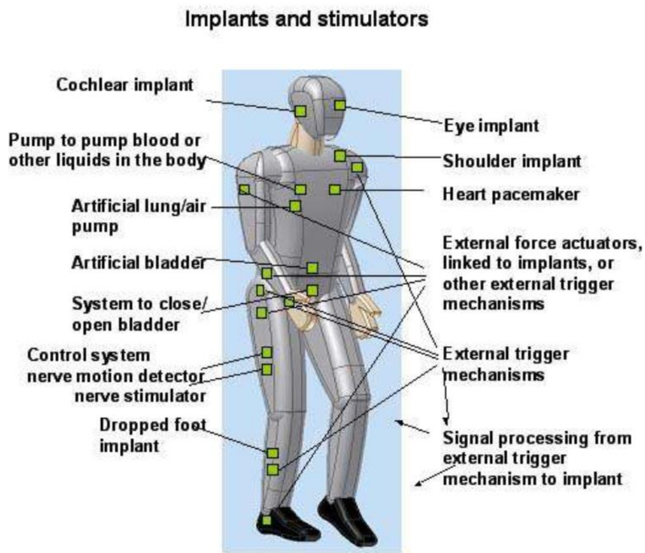

Figure 1.5: Depiction of the various implants and stimulators requiring sensors and actuators [7].

Another scenario that defines large opportunities and challenges for sensors and actuators is the one of implantable smart systems (see Figure 1.5).

Covering all the available technologies within one report is impossible. Therefore we will restrict ourselves to a specific subset. The characteristics are

- The devices are to monitor specific body signals, intermittently or continuously and linked to an individual. Therefore they are on or near the body, embedded in clothing or implanted for a certain period of time.
- They should be comfortable and unobtrusive. This set upper limits to their dimensions and weight. Typically they are in the order of mm to cm's. This is especially important for implanted devices
- The devices either store their data internally and are read out regularly, or they are wirelessly linked to a central hub (e.g. cell phone), which enables to share the data externally.
- The devices should be autonomous, which means that there should be sufficient energy available to operate the device during the required lifetime of the application. This can range anywhere from a few minutes to a few months.

As an important consequence of the requirements above, the power budget is limited. There are two solutions. Either the devices are battery operated or powered by energy harvesting. In case of battery operated devices, the maximum size of the device determines the available capacity of a battery. In case of energy harvesting, power is also limited despite many claims in literature. It is important to note that the cost price is an important factor here. MEMS technology enables to reduce the price of the harvesters considerably, but this is at the expense of power delivered (this will be treated in more detail in chapter 2). As a consequence, the power budget for these devices is directly limited from several μW's to a few mW's.

The focus will be put on three types of applications areas:

- **Stay fit**: Applications for the healthy people to enable them to become or stay fit
- **Get well**: Applications for people who suffer from a disease and where the applications can either treat or monitor.
- **A better live**: Applications for the chronically ill, increasing their quality of life.

These devices are being used for prevention (including the promotion of healthy lifestyle through fitness and stress monitoring), diagnostic purposes, therapy and therapy monitoring. They are used at home by the user, or enable the patient to be monitored or treated at home under supervision of a professional. In the latter case they act as kind of an extension of the hospital care.

Another important development is related to mHealth (m-health or mobile health), which is a term used for the practice of medicine and public health, supported by mobile devices. Currently the most important device is the mobile phone, or tablet. In the future, devices like wrist watches of Google glasses might become important as well. As a consequence, all the applications discussed in the report need to interface with these devices, connecting wirelessly using protocols like Bluetooth, WiFi etc. Once connected to these mobile devices, they take care of transferring the data to the user or the internet. As a consequence, the devices do not need to make contact to the internet by themselves.

1.4 Other activities

On various levels, the notion that healthcare and its spending can be benefitted from the use of microsystem received increased attention. A (non-exhaustive) list:

For years, the EU has funded developments in the Health arena. An overview of the activities in the FP5 and FP6 framework, was documented by Lymber and Dittmar [8]. In the FP7 framework, these activities have been continued (for example, "Wiserban" focusing on wireless sensor nodes [9]). In 2013, the budget for funded projects in the FP7 were budgeted at approximately € 650 Mln. For the new Horizon calls (for 2104 till 2020), in the theme “Societal challenges - Health, demographic change and wellbeing” the indicated budget is 8033 Million Euro [10]. 254 Million of this amount is labeled for the European Institute of Innovation and Technology (EIT).

In September, the European Technology Platform for Smart Systems (EPOSS), published a pre-print of their strategic research agenda [11]. The Health and personal wellbeing sector worldwide is immense in value: in 2011, $309bn (source: Vision Gain 2012) for the worldwide medical device sector, including $90bn for medical electronics. Currently Smart Systems account for possibly ~10 to 12 % of this, but could rise to ~40% of the $130bn of medical electronics (> €50bn) by 2020 through wider adoption of Smart Technology in each of the subsectors examined.

It is important to mention the fact, that technology alone will not be the only factor in reducing the cost of healthcare. The healthcare sector is the sector with the highest level of system inefficiency, but, at the same time the sector with the highest potential for improvement[12]. A multi-disciplinary approach is essential, since changes in medical science and technology, need to go along with improvement in social, economy and IT. A recently started FP7 funded project, called WeCare [13], tackles just that issue. The aim of this project is to bring together specialist in the various fields and define a research roadmap for the various fields. Again, the aim of this document is to look the technology side alone. The exact scope will be discussed in the next section.

1.5 Report Outline

A broad discussion of applications for the wearable and implantable smart systems is the core for Chapter 2. These applications can be divided in clinical and consumer wellness applications. The main requirements for these systems are discussed and we dive into the issue of powering the systems.

Chapter 3 gives an overview of a broad variety of technologies for the Sensors and Actuators that can be applied, discussing ExG, MEMS accelerometers and gyroscopes, bio-chemical sensors, sensors for gas and airborne particles, the sensor integration on patches and micro-pumps and actuators.

Chapter 4 is all about Sensor Electronics and Signal processing. It discusses some of the issues and solutions about the circuit design for the electronics, needed to read-out the specific signals coming from or close to the human body. After read-out, signals need to be processed, which is reviewed in the last part, all at the lowest power budget possible.

All the sensors, actuators and circuitry, i.e. the full system needs to be integrated and packaged into one module, which is the topic of Chapter 5. Integration of the functionalities (SoC vs SiP), flexible packaging, 3D chip stacking and (flexible) interconnects are discussed. Finally, some of the specific issues for implantable devices are presented.

The data needs to be shared with the outside world, which can be done by wireless communication or by storing it in memory (Chapter 6). Antenna design, different communication protocols and standards and RF-IC design issues are presented. Also data processing and data storage is discussed

Finally the user interface and sensor acceptance is addressed in chapter 7. A lot of data is generated but how is this translated into useful information for the user? Without proper interfacing, the user is either overloaded by data, or given non relevant information. Privacy and Big Data are of growing importance, as already is shown by the recent headlines in the news.

The report concludes with an executive summary, where all conclusions and recommendations are brought together and presented.

1.6 References

[1] OECD Health Data, http://www.oecd.org, accessed Jan 10, 2013

[2] http://www.reforminghealthcare.eu/economist-report/challenges-facing-healthcare-systems/demography-and-disease-load

[3] Chapin White, "Health Care Spending Growth: How Different Is the United States From the Rest of the OECD?", Health Affairs, 26, no. 1 (2007): 154–161

[4] Road traffic collisions-case fatality rate, crash injury rate, and number of motor vehicles: time trends between a developed and developing country, Goonewardene SS, Baloch K, Sargeant I:. Am Surgeon 2010, 76:977-981.

[5] http://www.iot-visitthefuture.eu/fileadmin/documents/researchforeurope/

[6] http://www.ga-project.eu/

[7] "MEMS and Sensors - emerging technologies and applications" Julian Gardner, Tutorial at ESSDERC/ESSCIRC, Bucharest 2013,

[8] Advanced wearable health systems and applications, Lymberis A, Dittmar A, IEEE Eng Med Biol Mag. 2007 May-Jun;26(3):29-33.

[9] http://www.wiserban.eu/

[10] http://ec.europa.eu/research/horizon2020/pdf/press/horizon_2020_budget_constant_2011.pdf

[11] http://www.smart-systems-integration.org/public/documents/publications/EPoSS%20SRA%20Pre-Print%20September%202013

[12] "The world's 4 trillion dollar challenge, Using a system-of-systems approach to build a smarter planet", IBM Institute for Business Value, January 2010.

[13] http://www.sahlgrenska.gu.se/english/news_and_events/news/News_Detail/gothenburg-coordinates-eu-project-on-reducing-healthcare-costs.cid1188041

Chapter 2 Application cases

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2.1 Overview

Application cases for smart systems can be broadly divided between systems designed and marketed for professional clinical scenarios and applications, and those targeting the consumer market, with the latter addressing more general health and wellbeing markets. In this chapter, a selection of applications will be reviewed, first those concentrated on the professional healthcare sector, then those which are more focussed on the consumer wellness market. The associated regulatory stringency requirements range from systems required for enabling clinical decision support, to devices and systems intended for the consumer market which promote wellness through informed lifestyle choices. The range of applications spans the full life cycle, from early pregnancy monitoring, through to monitoring in palliative care contexts. While business models for products for each market will differ significantly, as with the levels of complexity, modules required, etc., a common requirement for all is that the design of the system has to start and end with the patient /clinician / consumer as the end user, and an optimal model for innovation leverages inputs from researchers and engineers from **A**cademia, **B**usiness experts and **C**linicians. This "ABC ecosystem" ensures that devices developed will leverage innovation for clinical utility and commercial opportunity.

In order to contextualize the opportunity, scenarios will be reviewed for systems for clinical applications related to:

(a) Pregnancy and neonatal monitoring

(b) Critical care monitoring

(c) Clinical competency assessment

(d) Post procedure rehabilitation and monitoring

And for wellness applications:

(e) Informed health and wellbeing including healthy and active ageing

(f) Personal safety

(g) Enabling independent living for persons with intellectual / cognitive disabilities

2.2 Application scenarios for healthcare

2.2.1 Pregnancy and neonatal monitoring

While the market for pregnancy monitoring encompasses both clinical and consumer markets, the driver for both is the high value in ensuring the health of both the mother and the foetus. The primary aim is to enable early indication of any adverse changes in the health status of either mother or foetus, so that early intervention could prevent premature delivery, or other complication, with consequent risks of damage during that critical period of development. While the survival rate of premature babies has increased, due to better monitoring during pregnancy, significant mental and/or physical disabilities which can result from adverse events during the first weeks of life, lead to the requirement of a lifetime of support services, with consequent challenges for the families and healthcare systems. Therefore, systems are required which can provide ambulatory monitoring of pregnant women as they carry on their normal lives, as well as minimally invasive or preferably non-contact devices which can monitor vital parameters in the neonatal context.

Over 130 million babies are born world-wide every year, and almost 20% of these have complications, such as pre-eclampsia, spontaneous preterm birth and/or foetal growth restriction. Globally, over 500,000 women die of pregnancy related causes annually and 99% of these occur in developing countries (UNICEF.org). Improvements in perinatal care over the last two decades have ensured that maternal mortality is now very rare in the developed world. While newborn survival is higher than ever, pre-term babies and those who suffer asphyxia are susceptible to hypoxic ischaemic injury and can develop a permanent disability such as chronic lung disease, cerebral palsy, blindness or deafness. The lack of appropriate screening tests prevents appropriate monitoring and preventative interventions to those at risk. The direct healthcare costs to provide treatment for major pregnancy complications is estimated at US$45 billion annually.

Pregnancy monitoring could ideally be envisaged as a smart patch, which would provide for continuous monitoring of both biochemical markers from peripheral blood or interstitial fluids, and electrical (ECG) signals from both mother and foetus. While embedded software in the device would be required to identify potential issues and minimize the requirements for continuous data streaming, the monitoring of the data should be performed by the obstetrics support team (i.e. not the patient).

Neonatal monitoring is essentially performed in a critical care setting with the extra challenges of the very small size of premature babies, starting with babies born after 23 weeks who typically weight just a few hundred grams. Due to the underdeveloped status of many of the organs of these tiny babies, continuous close monitoring of movements, blood gases, colour, etc. is required. However, smart systems using non-contact and /or wireless telemetry methods for monitoring those vital parameters would be preferred to minimise the need for connecting or disconnecting devices each time the baby is handled.

In the typical scenario where the baby is within an incubator unit, there is a great opportunity to develop the incubator as a sensorised system with functionality on the system for non-contact monitoring, in the mattress and some miniaturised devices as wearables (where the latter should ideally have a minimal footprint and weight), and use a local area network to interface with the clinical monitoring system and data records archive.

Electronic systems for neonate monitoring such as EEG devices are required which can be minimally invasive, while maximizing monolithic integration of front end electronics for DSP to ensure data integrity, smart management of power, and wireless telemetry.

Similarly for EEG, the design of the electrodes and the device / adhesive used to hold the electrodes in place will also need to be optimised to minimise the effects of impedance due to movement of the electrodes.

Multidisciplinary approaches are required to address these needs where the research is clinically led, involving relevant industry partners, and focussed on addressing the need for more effective monitoring of pregnancy and newborn babies (e.g. the INFANT Centre - Irish Centre for Foetal and Neonatal Translational Research - www.infantcentre.ie).

2.2.2 Critical care monitoring

As healthcare systems move towards electronic records, this provides an opportunity to include more extensive monitoring of critical care patients especially. Currently in the critical care setting of an intensive care unit or high dependency unit of any hospital, several parameters are continuously monitored using standard instrumentation. The challenge for the clinical team in this setting is to identify potential adverse events in an environment where instrumentation is often continuously alarming based on parameter thresholds set for a standardised patient cohort. However, ideally, each patient on admission to hospital would be provided with some form of minimally invasive, wireless and wearable system which could track a range of physiological parameters, movement through the hospital, and progress during recovery and for an initial period following discharge (in line with preventing readmission based on the "Obamacare" model in the US). This sensing system could be envisaged as a set of wireless sensing devices for monitoring SpO2 (pulse oximetry), temperature, capnography, pulse, position, location, movement, etc. These sensors should communicate locally with a medical grade data aggregator, which would perform some analyses and alerts where applicable, and then stream the data to the patient record archive, for more comprehensive analysis and population level data analytics. This data would be a highly valuable asset for decision support during critical care monitoring, and potentially could enable an early move to step down care or discharge based on the confidence that any deterioration in condition could be quickly identified and the critical care monitoring and treatment programme quickly reinstated. Such patient centric monitoring would greatly enhance the quality of patient care, avoid repetitive questioning of the patient on basic details by hospital staff in different sections, and provide an opportunity for data analytics to interrogate the data at the patient level to identify longitudinal patterns which could be diagnostic or predictive, interrogate population data to identify such patterns using big data analytics, and help improve efficiency with the hospital environment by tracking movement of patients and their interactions with individual clinical staff. The potential exists for these sensing systems to use wireless charging based on inductive powering of integrated antennae, however the need to ensure no interference with all other instrumentation in the critical care setting is of paramount priority, and such systems need to be fully validated for all scenarios. There is also a need for local processing within embedded software to avoid the need for continuous streaming of all data, but ensuring that deviations outside of set thresholds can be rapidly identified and communicated to prevent adverse events.

2.2.3 Clinical competency assessment

To date, the education and training of clinical staff has been based on an apprenticeship type model, where a procedure is initially observed, then practiced under supervision, then independently, and finally that clinician becomes an instructor for that procedure. It has been very difficult to objectively assess the competence of individual clinicians other than by monitoring adverse outcomes. Smart systems provide a new opportunity to address the challenges of new regulatory requirements to monitor the performance of clinicians during each of the microtasks involved in performing a procedure. Precise monitoring of the movements of the clinician, his/her interaction with other members of the clinical team, monitoring of eye-gaze and an indicator of focus, physiological parameters as a measure of stress etc., all provide a new opportunity to enable an objective analysis of clinical competence (rather than the current subjective methods of basic observation of procedures and tracking of poor outcomes). Such monitoring when combined with simulation analysis using the new generation of virtual reality simulators, provides a basis for objective analysis of clinical performance.

Over the next decade, technology enhanced learning (TEL; including simulation) will change its role in the education, training and assessment of health professionals from peripheral or supportive to central and mandatory. One illustration of that fundamental change is contained in the recent (November 2011) UK Department of Health Framework document (Appendix 1) which " clearly states that healthcare professionals...should learn skills in a simulation environment and using other technologies before undertaking them in supervised clinical practice". This recent change in UK national policy is representative of the direction being taken across the developed world. Based on 2009 legislation, Australia has undertaken a $ (Aus)1.6 Bn investment in a new national approach to clinical education, to which an embedded simulation programme is central [$ (AUS) 100M will be spent before 2014 on new simulated learning environments].

There are five international drivers for the changes in government policy in relation to TEL/health, namely:

(a) Patient safety. One half of all patient adverse events are the result of an invasive procedure. The number of such events (at least in the US) has not decreased since publication of the Institute of Medicine's "To err is human" in 2000 [1]. Human error, amenable to correction through improved simulation-based training, is a dominant cause.
(b) Progressive decrease in clinical learning opportunities for health professionals (new explicit patient covenant, legislation such as EU Working Time Directive)
(c) Worldwide move from time-based to competence-based training in healthcare.
(d) Legislation which requires implementation of mandatory professional competence schemes (e.g. [2]). Current or future mandatory recertification/revalidation of health professionals.
(e) Medical "inflation" - increase in the rate of development of new techniques, procedures, devices with evidence of (or licensed to) improve patient care.
(f) The bodies responsible for licensing medical devices will require evidence of valid reliable forms of assessment of the use by individual practitioners. The FDA recommends validation and human factors testing in a simulated environment as part of any pre-market approval application [3].

It has become clear that a detailed “scientific” characterisation of a medical procedure could enhance its safety and efficacy through enhanced operator/team performance, better device integration and improved design of procedure “spaces” such as operating theatres. Medical errors occur commonly and often that i. result in patient harm or death, ii. are preventable, iii. are due to human error, iv. are associated with procedural healthcare (e.g. surgery) [4],[5] and iv. have proven difficult to eliminate despite substantial effort and investment [6]. Several helpful advances have been made over the past decade which could improve patient outcome associated with procedural healthcare.

These advances include:

(a) Development of a set of "metrics" which characterise quality of performance of a procedure.
(b) Application of these metrics to define a standard or set of standards for the procedure.
(c) Application of these metrics to develop a valid reliable assessment tool for the procedure.
(d) Structured simulation based training can result in improved clinical performance of a procedure. (e.g. (a)-(d) above [7],[8])
(e) Improved clinical performance is associated with superior patient outcome [9].

Taken collectively, we believe that these advances indicate that a detailed characterisation of a procedure (intended to identify and quantify those elements which deliver the end for which a procedure is intended) offers a means of improving patient outcome. This characterization needs to identify those parts of the procedure which determine whether it is successful and whether it is performed safely. Clearly defined these "metrics" can be used to distinguish between superior and inferior performance, underpin an effective training programme (proficiency based progression) in simulated and clinical environments, and this process should result in better patient outcomes.

The ASSERT for Health Centre in Ireland (http://www.ucc.ie/en/medical/assert/) has set out a standard methodology (framework) to employ some of these advances in combination to improve patient outcome associated with a procedure and ii. to implement this methodology for individual procedures.

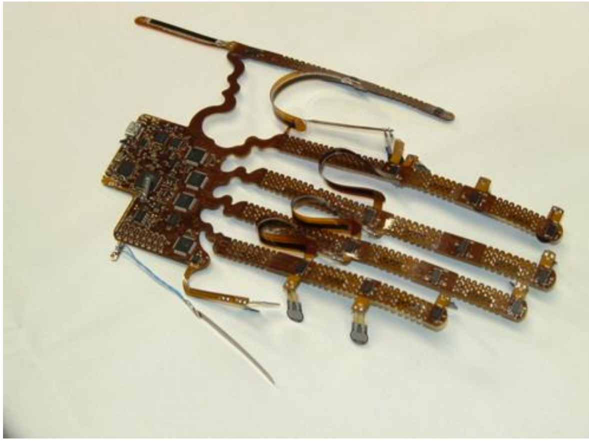


Figure 2.1: The human hand exhibits complex biomechanical movement with 15 individual segments that require mapping [32]. The above figure illustrates a wireless inertial sensor glove developed by the Tyndall National Institute and employed in a range of applications including empirical studies involving surgical training and rehabilitation

Based on the above requirement to enable new solutions for objectively measuring clinical competence, and the need to facilitate training for new medical devices and procedures, there is a clear need for a wide range of "smart" functionality to be integrated onto typically inert surgical tools, to precisely monitor movements, identify surrounding tissues, measure physical, chemical and biochemical parameters, and monitor various movements and behaviours of the clinical team and their environment. All this data needs to be streamed wirelessly and data fusion enables detailed analysis each microtask of the procedure, the performance of the lead clinical during the procedure and the interaction of the clinical team with each other and their environment. This will require a range of nanosensing platforms integrated in form factors appropriate to a range of surgical devices, with wireless telemetry, packaged in biocompatible materials, and with energy sources and management as required for the duration of the procedure. An additional challenge is that many of the devices will need to be disposable to ensure sterility, and therefore the system design will need to take account of stringent cost constraints.

2.2.4 Post procedure rehabilitation and monitoring

As mentioned earlier, and in line with the reimbursements penalties associated with readmission within 30-days, there is an increasing need to ensure the continuum of care necessary to avoid unnecessary post procedure complications.

The word rehabilitation is derived from Latin *rehabilitare*, which means 'to make fit again'. According to WHO, the World Health Organisation, rehabilitation refers to deliberate medical, social, pedagogical, occupational, and technological measures, as well as inadvertent influences of the rehabilitee's social networks and physical environments, that should enable him or her to perform functional activities as well as possible [10]. Medical rehabilitation is essentially a treatment or treatments designed to restore, as fully as possible, to an individual, disabled through an injury, illness, disease, and/or chronic disorder, his or her lost or impaired abilities and skills and/or to compensate for those by developing his or her residual ones. The most basic of these abilities and skills include walking, driving, learning, and grocery shopping, and many medical rehabilitation facilities today offer suitable training programs.

One particular branch of growing significance is orthopaedic rehabilitation. In a survey conducted by the European Agency for Safety and Health at Work in the 27 EU member countries, approximately 25% and 23% of employed respondents reported having work-related back and muscle problems respectively, which made musculoskeletal injuries or disorders the most often mentioned occupational illnesses [11]. The phenomenon of the "ageing society", that is of the anticipated growing life expectancy in Europe in general and Germany in particular, indicates a long-term growing demand for rehabilitative services. Be-tween 2006 and 2020, the number of rehabilitation cases in Germany is expected to increase by 6.3% overall, or by 0.43% annually. In certain areas such as neurology, cardiology, haematology, orthopaedics, clinical geriatrics, and medical oncology, a considerably greater increase is expected [12].

As the number of medical cases increases, medical expenditures per citizen will be proportionally reduced. Health care providers such as medical facilities, state insurance, and national social security funds will respond with longer waiting lists, shorter treatments, and higher deductibles. The proportion of inpatient treatment will considerably decrease in relation to outpatient treatment, and the individuals will be obligated to take more responsibility for their health. The health care focus is expected therefore to shift from "post-facto" intervention to prevention, as emphasized by the German state retirement fund [13]. Furthermore, because of the "ageing workforce" and expected shortages of skilled labour in certain industries, it is expected that companies will find it increasingly useful to contribute to maintain the good health of their employees. Finally, each individual in particular and society as a whole will have to take more proactive stands toward health. In the clinic, all data are archived in a medical documentation system and when the attending physician or therapist is using the so called therapist environment, s/he can access all these documents. The therapist workstation can be used to monitor the state of health of the patients, it can be used for editing the exercise and therapy plans, it has integrated – text or video based – communication facilities and it is used for documenting the therapy progress. When a patient leaves the clinic, they are provided with therapy or training plans which comprise of personal data (name, age, diagnosis, therapy and training goal), information about the kind of exercises (e.g. combination of Nordic walking, walking, and stretching), and information about training duration and length (e.g. training intervals and order of exercises). Depending on the actual therapy progress, the attendant physician or therapist should modify the training plans on a regular basis. One major concern of the project is the secure transmission of data between the different involved components, and another is, that the system easily can be connected to an existing IT infrastructure of a rehabilitation centre.

The demographic evolution in the European Union and the increasing number of chronic diseases will trigger a paradigm shift. These developments will lead to rising costs for medical treatment and rehabilitation, and the politicians and purchasers will ask the providers of medical services to reduce expenses and to prove that they offer efficient care. Beside the necessary rehabilitation measures in the future prevention measures and preventive medicine will appreciate a greater focus. The primary task of telematics in the health care system is to enable cross-sectoral services and an optimal communication between health care providers and purchasers. The focus of future developments must be to tune the systems individually to the capabilities of patients, where the attending physician or therapist creates a precisely fitting therapy or training plan, which then is carried on and modified autonomously by the trainee. While training autonomously, the trainee instead should get feedback on the sequence of movements, on vital data, and on the overall training results.

In recent years, the versatility (robustness, miniaturisation, usability) of the needed technology (body area networks, optical sensors, mobile devices, multimedia PCs) advanced very much. The tremendous progress in microsystems engineering allows sensors to be employed in mass applications more and more. Accordingly, the technical entry barriers for an extensive usage of tele-rehabiliation services are low. With respect to the necessary data integration of different medical information systems running standardization projects like the Continua Health Alliance or HL7 are developing promising interoperability standards. Future tele-rehabilitation services can be implemented on top of these standards.

2.3 Application scenarios for wellness

2.3.1 Informed health and wellbeing including healthy and active ageing

Stress

Stress is a major problem in society; in 2007, 8.6% of the European people aged 15 to 64 years that work or worked previously, suffered from one or more health problems caused or made worse by work in the past 12 months [14] The second most frequently occurring type of work-related health problem in 2007 was 'stress, depression or anxiety', which was reported by 13.7% of the workers as the most serious problem [14]. This corresponds to over 3 million persons in Europe. Of the sickness absence for one month or more in 2007, 25% was caused by stress, depression or anxiety [14]. In the US, 30–40% of employees report their job as stressful and the number of lost work days due to anxiety, stress, and neurotic disorders is four times higher than other nonfatal injuries and illnesses [15].

In order to start stress prevention, people should be aided in becoming aware of stress. People who experience stress do not always change their way of working. They do not make enough effort to release stress, or they are not aware how to reduce stress. Therefore, it would help them if they would get a stress indicator, real-time. Experiments [16] have been carried out to calculate a relative stress level, by measuring physiological parameters and translating this into a single stress estimate. In the lab, sensors were attached to the body (on 30 subjects), measuring the Electrocardigram (ECG), the respiration (RSP), the skin conductance (Electrodermal activity, EDA) and the Electromyogram (EMG) at the Trapezius muscles. From the signals, the relevant features were extracted, the signals were normalized and specific features were selected. Both linear and logistic regression were used to construct continuous stress measures. An example of the result is shown in Figure 2.2.

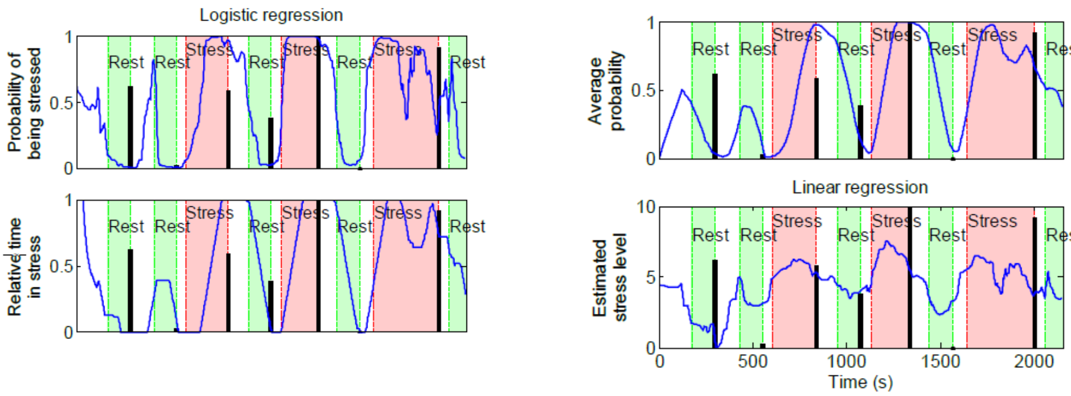


Figure 2.2.Example for one of the subject's signals, showing the stress levels estimated using logistic and linear regression. Black bars show subjective stress levels indicated by the subject. [16]

From the results it was concluded that a value of around 80% for the stress determination can be reached.

Fitness

Lack of physical activity is one of the major health problems in most of the western world. Even though our genome has not changed much over the last ten thousand years and more [17], activity patterns of our hunter-gatherers ancestors have been first modified by the agricultural and industrial revolution, and then completely disrupted by the shift towards computer-based work which took place over the past twenty years. As a result, two thirds of the world population is overweight and obesity affects a third of the population in the US at present. It is estimated that 31% of the adults aged 15 and over are insufficiently active. Worldwide, there are 1billion overweight people, and 3.2million deaths each year are linked to insufficient physical activity. Overall, this is the 4th leading risk factor for global mortality. In the US alone, the direct costs from obesity are $160 billion, and indirect costs are $450 billion [18].

Other diseases, such as diabetes, are rapidly becoming widespread epidemics as well [19]. Accurate quantification and assessment of habitual physical activity in ambulatory settings is essential in order to find subtle but important links between not only sedentary time, but all the aspects of habitual physical activity, and health [20]. New technologies, seamlessly integrated in everyone's life, able to monitor objectively and non-invasively our behaviour, can provide unprecedented insights on these links.

The physical activity is directly related to the Energy Expenditure, which is the sum of internal heat produced and external work done by an individual. The Cosmed K4b^2 device has been found to be a valid and accurate device to measure energy expenditure in prior studies [21]. The system consists of an apparatus that measures oxygen uptake (VO2) and carbon dioxide (VCO2) production by means of a face mask. VO2 values (in ml/min) can be converted to resting metabolic equivalents (METs) by dividing by the subject body weight and 3.5 (One MET is equivalent to 3.5ml of VO2 per kilogram per minute). The device weighs less than 1kg and is composed of a face mask, a data collection unit, and a rechargeable battery. The data collection unit and battery pack were affixed to the participant's chest using a special harness consisting of adjustable belts.

Clearly, such a system cannot be used for daily use. Therefore, many devices have appeared on the market that are much smaller and much more comfortable, while still claiming to measure activity levels. All these devices are to be worn on the wrist, or attached to the body. They all measure movement of the person by accelerometers, and some even give the user a value of calories burned. However, this value is very difficult to determine with these rather simple devices. Also, the autonomy of each devices is limited, being anywhere between 2 days and 2 weeks.

A methodology for activity-specific Energy Expenditure EE algorithms has been developed by [22]. The proposed methodology models activity clusters using specific parameters that capture differences in EE within a cluster, and combines these models with Metabolic Equivalents (METs) derived from the compendium of physical activities. A protocol has been designed consisting of a wide set of sedentary, household, lifestyle and gym activities, and developed a new activity-specific EE algorithm applying the proposed methodology. The algorithm uses accelerometer (ACC) and heart rate (HR) data acquired by a single monitoring device, together with anthropometric variables, to predict EE.

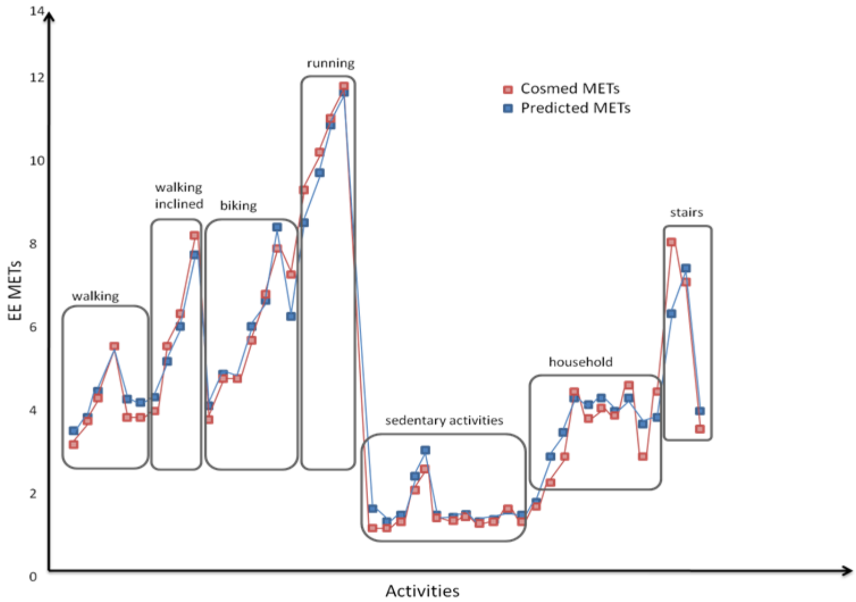


Figure 2.3: Comparison to the developed EE MET's estimate and the result from the Cosmed system

Increases in EE estimation accuracy ranged from 18 to 31% compared to state of the art single and multi-sensor activity-specific methods. A very good agreement between the data obtained from the Cosmed system and the predictions using the algorithm can be seen (Figure 2.3)

2.3.2 Personal Safety

One of the main interests of people is their personal health and wellbeing. Consequently, gadgets that provide safety and hazard information are in great demand with the general public. For instance, 180 U$ is acceptable for a simple metal smartphone casing to protect from radiation. In this context, next generation technologies that provide information on environmental pollution and related health risks have started to emerge [23]. The related market segment of environmental sensors and monitoring was valued globally at $11.1 billion in 2010 and is expected to reach $15.3 billion in 2016, a compound annual growth rate of 6.5% between 2011 and 2016.

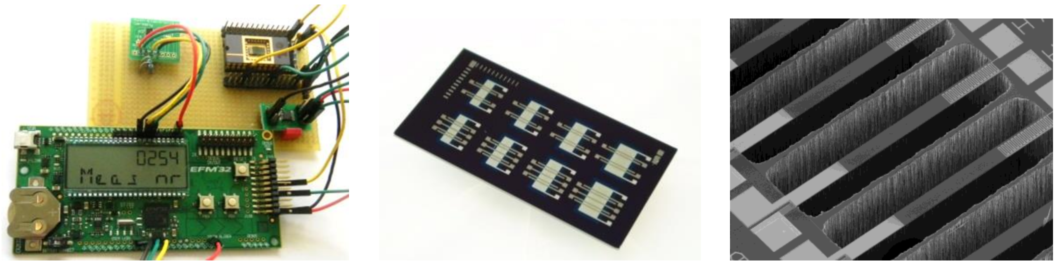


Figure 2.4: Pictures of environmental sensor solutions being developed [21]. Left: NO2 sensor in a DIL package connected to a circuit. Middle: Metal oxide based sensors in a FET configuration. Right: MEMS-Resonators used to monitor volatile concentrations.

The next large step forward will be the development of miniaturized pollution monitoring solutions that can be integrated in wearables (e.g. wrist watch). When such devices are able to upload their information, distributed sensors from many users would enable real-time mapping of air pollutants, providing a vast improvement compared to the small number of fixed monitoring stations employed today.

In this context, a miniaturized low power chemical sensor solution with superior selectivity is developed. A good example suitable for pollution monitoring is a NO2 sensor based on an AlGaN/GaN heterojunction that reaches ppb level sensitivities and shows a high level of selectivity to other gases such as SO_2, C_2H_4, CO_2, etc. For indoor air quality CO and CO2 sensing solutions have been developed based on metal oxides that can operate at significantly lower temperatures (or even room temperature) in order to reduce power consumption and thus enable implementation on autonomous systems.

In contrast, for detection of volatiles that have a significant influence on our wellbeing, a MEMS-resonator based electronic nose has been developed that relies on stress induced frequency changes of polymer coated resonators. Here, an array is used where each resonator is coated with a different polymer and each is sensitive to a large number of volatiles, but all in a somewhat different way. Using principal component analysis, one can then extract information on volatile pollution, despite the lack of selectivity of the individual polymers.

2.3.3 Enabling independent living for persons with intellectual/cognitive disability

There is a significant challenge for technology to enable independent living for persons with a wide range of physical and intellectual disabilities. While modern healthcare enables people to live significantly longer, their physical and intellectual condition in the latter years, can compromise the ability to live independently without additional supports. Similarly, there is a clear consensus and regulatory requirement that people with intellectual disabilities should be facilitated to live in the community rather than reside within institutional care. While in many cases palliative care is only possible within the supports available in a hospice, the opportunity to enable people with terminal illnesses to spend as much of their final moments in their home, presents a technological challenge. While there are obviously very clear differences in the aforementioned scenarios, there is a common need for new technologies for continuous monitoring, and remote telemedicine type supports to replace the level of care that would otherwise require the people involved to reside in residential care. The health economics of enabling independent living are clear cut. Care support for someone living at home may cost in the region of €2000 per month, while residential institutional care would typically cost around €1000-2000 per week. Acute care in contrast would cost in the region of €2000 per day. So the challenge from a simple economic perspective, is to provide the support necessary to maintain people in their own homes in the community, and to prevent adverse events e.g. falls, which result in requirements for acute care, and / or long term residential care. Given the escalating healthcare costs (See Figure 1.1) and increasing elderly population, new technologies and approaches are essential to maintain healthcare systems in all countries.

Figure 2.5: A participant to the multi-sensor Activities of Daily Living recording at the Greek Alzheimer's Association in Thessaloniki (Feb. 2013) (http://www.demcare.eu/)

Emerging technology solutions are providing the opportunity for remote monitoring and telemedicine which will greatly facilitate the opportunity for independent living. However, significant technological challenges still remain. One critical factor is that many solutions are unacceptable to the end user, as they are too obtrusive, inconvenient, appear to confer some sort of unacceptable negative label on the user, or require too much maintenance for routine use (see e.g. Figure 2.5). There is a clear need for design of devices which facilitate independent living to be carefully contextualised with end users, such that unintended perceptions or overseen issues can be addressed in the product design from the outset. In general, devices will need to be minimally intrusive to the appearance and lifestyle of the person, be compatible with power harvesting to avoid the need for regular recharging, and where applicable, they need to be in a form factor appropriate to being in direct contact with the body either as a wearable or implantable device. Non-contact measurement of vital signs would be of great advantage, and creative form factors are required which exploit everyday utilities to gather essential data on their health and wellbeing e.g. smart watches, rings, patches, dentures, etc. In particular, minimally invasive devices on or near the person, which can detect deviations from normal movement patterns should be developed.

2.4 Requirements

The diversity of applications envisaged means that it is challenging to make definitive statements regarding the requirements which would be applicable across the range of scenarios. However, clearly there is a need for these systems to get to a point where cost of the device becomes negligible, the size and embodiment makes them almost invisible, installation is automated and no maintenance is required. There are many examples of current devices which function well technically, but are not acceptable to or suitable for the end user due to complexity, size, perceptions of social stigma, etc. (see Figure 2.6 for an example of some available products). Therefore, a detailed engagement with end users is required to understand the priorities of the design team, where compromises may be required e.g. size against performance. In some cases, system can be miniaturised to millimetre scale devices, using monolithic IC integration to combine sensing, processing, power, communication, etc. However, some of the interfaces either for sensing of the body or for the user interface require larger scales, and where possible, these should be typically be in on flexible substrate. In many cases, the devices may be designed to perform measurements for a fixed period of hours, days, weeks or even months, and then some or the entire device should be disposed. Therefore, where practical and without compromising performance, low cost disposable materials should be adopted within the disposable modules during design, to ensure that functionality is blended with compatibility for the end user requirements. Therefore, essential requirements include low cost, disposable modules to facilitate hygiene, scale/ergonomics compatible with the use case scanerio and related social considerations, avoidance of any installation or maintenance needs, and the ability to engage the end user in a positive way for using the device /system (regardless of whether the data is made available directly to the end user or to the clinical support team.

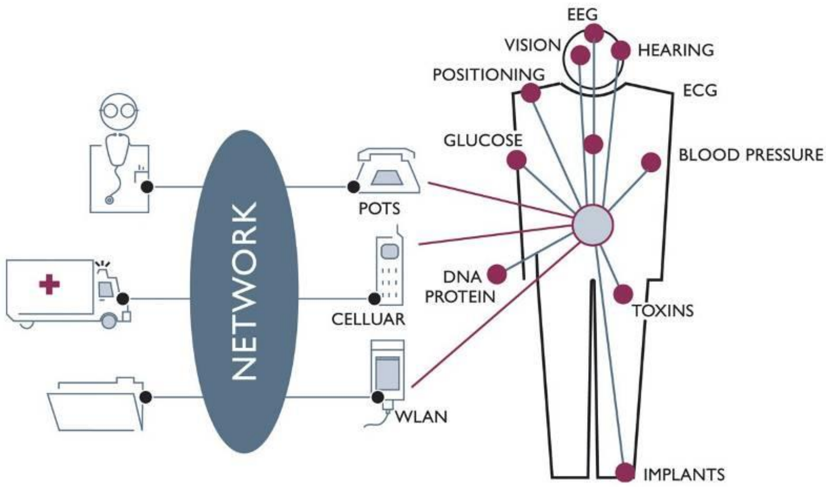


Figure 2.6: Basic schematic of the Body Sensor network. On-body or implantable sensors measure parameters, and send these to the outside world through a network connection.

Powering the sensors: Energy Harvesting or batteries

The use of wireless devices automatically means that power cannot be delivered by the mains. Either batteries need to be used or alternatively energy harvesting: a technology that extracts unused energy from the ambient and converts it into useful electrical current and voltage. Energy harvesting is a topic which has attracted a lot of interest, especially in recent years. Already in 2008 a previous Catrene report discussed the status and outlook of energy harvesting, in a report dedicated to wireless sensor networks [24]. Although very appealing, energy harvesting has its limitations. In order to be economically competitive, harvesting devices need to be produced using micromachining technology. As a result, power is determined by its physical dimensions. Depending on the exact physical phenoma used, power levels vary over more than 4 orders of magnitude. For example, a PV cell used outdoors, can easily provide 10mW/cm², while RF energy harvested from the ambient will deliver in the order of 0.1μW/cm² [25].

From the battery point of view, one can state that if an average power of 100μW (10μW) is needed, battery lifetime of a 1 cm³ volume battery can be estimated to be around 20 (200) days [25]. It has been reported that the energy density increase of batteries has been limited to a factor of two to three per decade [26]. However, many recent publications have claimed improvements in materials or new device concepts that may lead to an accelerated energy density increase. This will affect the application window for wireless sensor nodes. However, care has to be taken to interpret some of the claims stated in research papers, as many of the properties reported are only valid for subparts and not for complete packaged battery systems. As is shown in [27], the energy densities for micro batteries, thin film and 3D batteries, although increasing faster than the macro batteries, the actual values of energy densities still are, and for many years, still will be considerably smaller than macro batteries (plotted in 2.7)

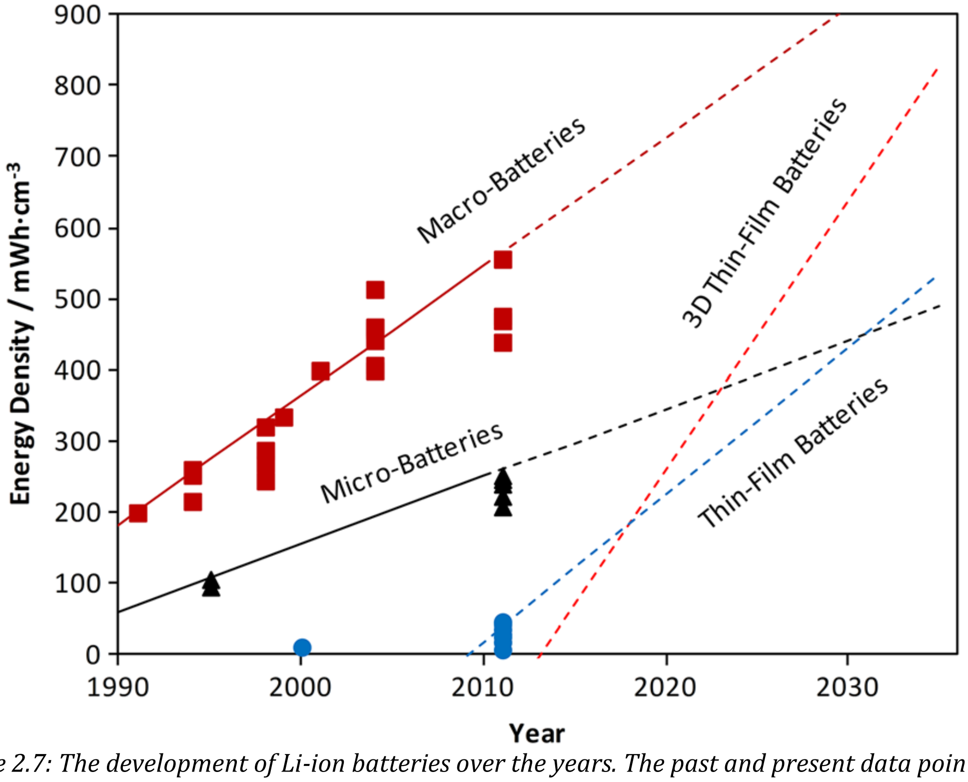


Figure 2.7: The development of Li-ion batteries over the years. The past and present data points are based on manufacturer datasheets and scientific literature. The future trends are based on the extrapolation of observed past trends and estimates of chemical and material science developments in the future (from [17])

Depending on the application of wireless devices, the required autonomy is different. In Figure 2.8, the required autonomy for the main wireless sensor applications is plotted. For example, for application within buildings ("smart buildings"), the lifetime should be up to 30 years. On the other side of the spectrum are applications for the wearable BAN devices. Typically, these applications only require a lifetime of 10 to 20 days. For implantable however, the required autonomy can be several years. In the same figure, the autonomy provided by a battery of $1cm^3$ is plotted. For 100µW need, the lifetime is 20 days, whereas for 10 µW devices, up to 200 days can be reached [27].

The choice between energy harvesting or batteries, is a result of an equation with has as parameters size, power and energy need and the energy to be harvested available. In practice, whenever the power need is such that it can be delivered by a battery, a battery will be preferred above an energy harvester. As the battery is a proven technology, the cost for a battery solution is far less than for a harvesting system.

Returning to the focus of our report, one can state that wearable body area network applications typically last between 1 week and 1 month. The electrodes will be disposable, whereas the electronics can be reused. Rechargeable batteries will be able to provide the necessary power when these are integrated in the reusable part. If these devices are to be reused, then there will be ample time to recharge the batteries. This will be simple and straightforward. Energy harvesting, although technically feasible, will increase the lifetime to infinity, but also the cost of the device will increase. It is therefore to be expected that in the majority of the cases batteries will prevail.

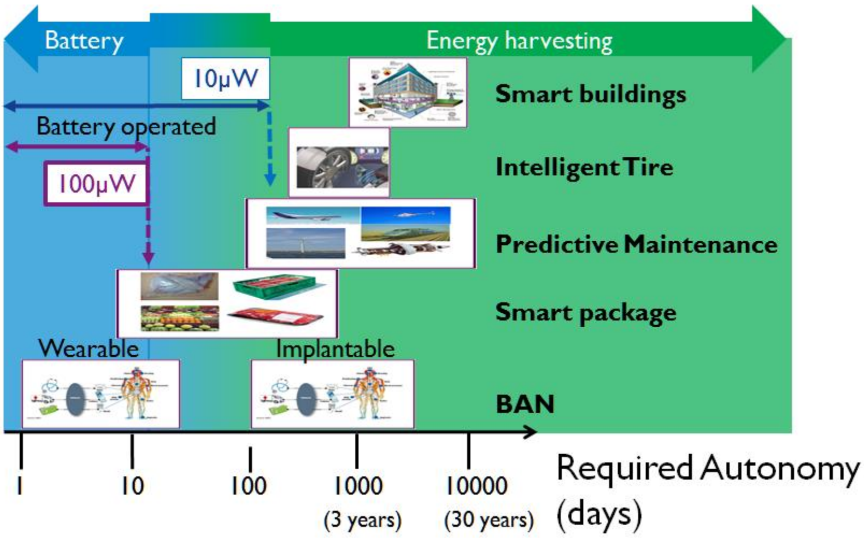
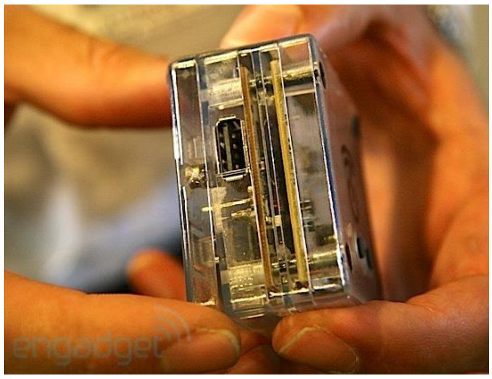


Figure 2.8: The application areas of smart sensors and their required autonomy. Also indicated is the lifetime of a $1cm^3$ battery, when delivering 10 or 100 µW of power (based on data from [27])

For implantable devices, the situation is clearly completely different. As the required autonomy is much larger, the classical recharging of batteries is not obvious. The non-radiative inductive principle from a short distance is a well-known technique for charging and reading out human-body implant devices. A rule of thumb is that the maximum distance is in the order of the dimensions of the coupled inductive coils. Radiative RF systems would extend the operating distance for wireless charging, for remote controlling the implants, and for reading out the implant device sensor data [28][29]. Small-sized applications will need small-size antennas for both harvesting and communication purposes. Combining the antenna for wireless communication with the antenna for RF harvesting into one small-sized system is a challenge. Examples of commercial available devices are presented in Figure 2.9



(a) (b)

Figure 2.9: State-of-the-art commercial long distance RF harvesting systems: PowerCast [30](a) and Ossia [31](b).

2.5 Outlook

Overall, there is a vast opportunity for leveraging nanoelectronics design and manufacture capabilities and infrastructure in to this rapidly growing market, to provide disruptive solutions for health and wellbeing applications. Successful products will require multidisciplinary approach involving an "ABC ecosystem", which combines academic, business, clinicians and patients / consumers.

2.6 References

[1] Landrigan CP, Parry GC, Bones CB, Hackbarth AD, Goldmann DA, Sharek PJ. Temporal trends in rates of patient harm resulting from medical care. New England Journal of Medicine. 2010;363:2124–2134. doi:10.1056/NEJMsa1004404

[2] Irish Medical Practitioners Act 2007 (http://www.irishstatutebook.ie/2007/en/act/pub/0025/)

[3] FDA draft guidance January 2012. (http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ProposedRegulationsandDraftGuidances/default.htm)

[4] Wilson RM, Harrison BT, Gibberd RW, Hamilton JD. An analysis of the causes of adverse events from the Quality in Australian Health Care Study. Med J Aust. 1999 May 3;170(9):411-5.

[5] Shojania KG, Thomas EJ. Trends in adverse events over time: why are we not improving? BMJ Qual Saf. 2013 Apr;22(4):273-7. doi: 10.1136/bmjqs-2013-001935.

[6] What went wrong with the quality and safety agenda? An essay by Michael Buist and Sarah Middleton. *BMJ 2013; 347 doi: http://dx.doi.org/10.1136/bmj.f5800*

[7] Seymour NE, Gallagher AG, Roman SA, O'Brien MK, Bansal VK, Andersen DK, Satava RM. Virtual reality training improves operating room performance: results of a randomized, double-blinded study. Ann Surg. 2002 Oct;236(4):458-63; discussion 463-4.

[8] Howells NR, Gill HS, Carr AJ, Price AJ, Rees JL. Transferring simulated arthroscopic skills to the operating theatre: a randomised blinded study. J Bone Joint Surg Br. 2008 Apr;90(4):494-9. doi: 10.1302/0301-620X.90B4.20414.

[9] Birkmeyer JD, Finks JF, O'Reilly A, Oerline M, Carlin AM, Nunn AR, Dimick J, Banerjee M, Birkmeyer NJ; Michigan Bariatric Surgery Collaborative. Surgical skill and complication rates after bariatric surgery. N Engl J Med. 2013 Oct 10;369(15):1434-42. doi: 10.1056/NEJMsa1300625.

[10] WHO, Health Topics Rehabilitation, http://www.who.int/topics/rehabilitation/en/, last visit 06.06.2012.

[11] European Agency for Saftey and Health at work, Arbeitsbedingte Muskel-Skelett-Erkrankungen: Präventionsbericht, Factsheets (Ausgabe 78, Februar 2008) Bilbao, Eigenverlag 2008.
[12] Augurzky, B. et al, Reha Rating Report 2009, Rheinisch-Westfälisches Institut für Wirtschaftsforschung, RWI: Materialien, Heft 50
[13] Prävention vor Rehabilitation", http://www.deutscherentenversicherung-bw.de/DRVBW/de/Inhalt /Presse/Pressemitteilungen/PM_2011/VertreterversammlungDez2011.html?nn=57866.
[14] Eurostat, Health and safety at work in Europe (1999-2007), 2010. ISBN 978-92-79-14606-0, doi: 10.2785/38630
[15] Stress...at work, DHHS (NIOSH) Publication No. 99–101, National Institute for Occupational Safety and Health (1999), at http://www.cdc.gov/niosh/docs/99-101/pdfs/99-101.pdf accessed on Dec 12th, 2012
[16] Wijsman, J.L.P.; Grundlehner, B.; Liu, H.; Penders, J.; Hermens, H.. Towards continuous mental stress level estimation from physiological signals, 16th world congress of psychophysiology. September 13-17 Pisa, Italy, 2012.
[17] L. Cordain, A. Gotshall, and S. Eaton. Evolutionary aspects of exercise. World Rev Nutr Diet, 81:49-60, 1997.
[18] McKinsey Quarterly, internet report, http://www.mckinseyquarterly.com/newsletters/chartfocus/2011_01.htm, accessed on Jan 7th, 2013
[19] S. H. Wild, G. Roglic, A. Green, R. Sicree, and H. King. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care, 27(10):2569, 2004.
[20] S. J. Marshall and E. Ramirez. Reducing Sedentary Behavior : A New Paradigm in Physical Activity Promotion. American Journal of Lifestyle Medicine, 2011.
[21] J. E. McLaughlin, G. A. King, E. T. Howley, D. R. Bassett, and B. E. Ainsworth. Validation of the COSMED K4 b2 portable metabolic system. International journal of sports medicine, 22(4):280-284, May 2001SSI paper
[22] M. Altini, J.Penders, and O, Amft, "Energy Expenditure Estimation Using Wearable Sensors: A New Methodology for Activity-Specific Models"'; Wireless Health 2012, October 23-25 San Diego, USA, 2012
[23] .Nima Nikzad, Nakul Verma, Celal Ziftci, Elizabeth Bales, Nichole Quick, Piero Zappi, Kevin Patrick, Sanjoy Dasgupta, Ingolf Krueger, Tajana Šimunić Rosing, William G. Griswold, *Wireless Health '12*, Month 1–2, 2010, San Diego, CA, USA.
[24] Energy autonomous systems: future trends in devices, technology, and systems CATRENE Working Group on Energy Autonomous Systems 2009, CATRENE, Bellevile, M., Cantatore, E., Fanet, H., Fiorini, P., Nicole, P., Pelgrom, M., Piguet, C. ,Hahn, R., Van Hoof, Ch., Vullers, R., Tartagni, M.
[25] Vullers RJM, van Schaijk R, Doms I, van Hoof C, Mertens R. Micropower energy harvesting. Solid State Electronics 2009; 53:684–693.
[26] Paradiso JA, Starner T. Energy scavenging for mobile and wireless electronics. IEEE Pervasive Computing 2005; 4:18–27. doi:10.1109/MPRV.2005.9.
[27] A review of the present situation and future developments of micro-batteries for wireless autonomous sensor systems, JFM Oudenhoven, RJM Vullers, R Schaijk, International Journal of Energy Research 36 (12), 1139–1150
[28] S.Y. Hui, "Planar Wireless Charging Technology for Portable Electronic Products and Qi", Proceedings of the IEEE, Vol. 101, No.6, June 2013, p. 1290-1301

[29] H.J. Visser, R. Vullers, "RF Energy Harvesting and Transport for Wireless Sensor Network Applications", Proceedings of the IEEE, Vol. 101, No.6, June 2013, p. 1410-1423

[30] www.powercastco.com

[31] www.ossiainc.com

[32] [10] Brendan O' Flynn, Javier Torres Sanchez, Philip Angrove, James Connolly, Joan Condell, Kevin Curran. Wireless smart glove for arthritis rehabilitation. 05/2013; In proceeding of: Body sensor networks, At MIT, Cambridge, USA.

Chapter 3 Sensors and Actuators

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3.1 Introduction: smart sensors and actuators for improved Quality of Life

In this chapter some selected topics from the wearable and implantable smart systems scenarios are addressed, with the main focus on the first ones, which encompass solutions with a reduced degree of invasiveness. However, as the frontier between an invasive and non-invasive smart system is frequently difficult to precisely define, the chapter includes some relevant emerging sensors for implantable smart systems, especially where the respective research is advanced in Europe and/or the potential economic and/or societal impact is large.

Therefore, the chapter is organized and addresses the following sections:

- Electro-physiological sensors (ECG, EMG, EEG, EOG) and electrodes
- MEMS sensors for human physical activity: accelerometers and gyroscopes
- Bio-chemical sensors
- Sensors for gas and airborne particles
- Integration on patches
- Micro-pumps and actuators

3.2 Electrophysiological sensors

Wearable sensors allow the continuous monitoring of a person's physiology with unobtrusive devices. More invasive sensors can be needed for treatment of dedicated pathologies (such as CNS and peripheral nerve stimulation), for such therapies implantable electrodes are used and active medical device technology.

3.2.1 Wearable electro-physiological sensors

Wearable health-monitoring systems have drawn a lot of attention from the research community and the industry during the last decade as is illustrated by the numerous and yearly increasing scientific publications and industrial publicity. A variety of systems – both prototypes and commercial products- have been fabricated in the course of recent years, which aim at providing real-time information about certain aspects of the health condition of the subject, and at alerting the subject in case of threatening conditions. Such wearable systems for health monitoring can be used for measuring significant physiological parameters like *heart rate, blood pressure, body and skin temperature, oxygen saturation, respiration rate, electrocardiogram*, etc.

In this section the focus is put on ***electro-physiological sensors***.

State of the Art

Electrophysiological information is based on the recording of weak electrical signals voltage generated by body organs. The voltage variations are recorded by electrodes in contact with the skin. Examples of biosignal are given in the following list:

- Electrocardiogram (ECG): electrical activity of the heart; the heart rate and it's variability can be extracted from ECG signal
- Electroencephalogram (EEG): measurement of electrical spontaneous or evoked brain activity and other brain potentials
- Electromyogram (EMG): electrical activity of the skeletal muscles (characterizes the neuromuscular system)Electrooculogram (EOG): measurement of the resting potential of the retina and the potential related with eye movements

All these signals have their own typical characteristics regarding amplitude and frequency (see Figure 3.1), which will influence the suitability of a recording system towards a certain biopotential signal. An EEG recording system needs to be much more sensitive and less susceptible to noise, since the EEG signals have a small amplitude. ECG signals are much stronger and hence easier to record, certainly if only the monitoring of the heart beat is important. In case details of the electrical pacing signals of the heart are essential, less noise can be tolerated and higher quality recording systems are essential.

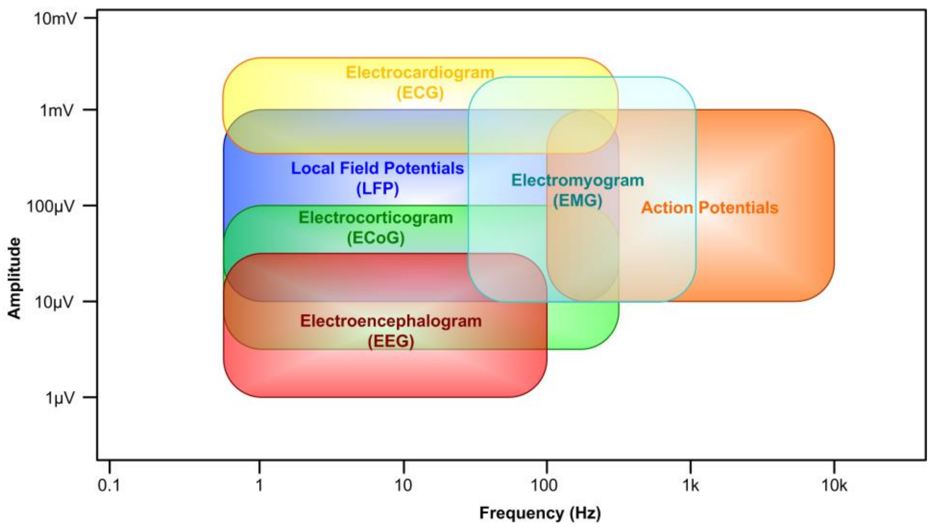

Figure 3.1 : typical amplitude range and frequency range of biopotential signals

The principle technical difficulty in measuring bioelectric signals from the body, such as electroencephalogram (EEG) and electrocardiogram (ECG), lies in establishing good, stable electrical contact to the skin. Traditionally, measurements of human bioelectric activity use resistive contact electrodes, the most widely used of which are 'paste-on' (or wet) electrodes. Wet electrodes are in direct contact with the skin, they use a conductive gel in order to enhance the skin contact and to lower the skin impedance by hydration of the stratum corneum (the top layer of the skin, which has the highest impedance). Although the skin-electrode impedance is low by using conductive gel, which results in high quality biopotential recordings, the use of wet gel electrodes has important disadvantages.. For ECG recodings, electrodes are mounted on the chest using adhesive tape. For longer time monitoring (more than a few hours) his tape is often cited as uncomfortable for the subject since it can lead to considerable irritation of the skin over time. For EEG recordings, the presence of hair on the scalp is a nuisance for the electrode mounting and dismounting. The so called 'cup-electrodes' are glues with special glue into the hair, as close to the skin as possible, followed by filling the cups with conductive gel to realize electrode-skin contact. The mounting of such electrodes takes some time (easily 1 hour for 20-30 electrodes), and removal of the electrodes is even more time consuming and painful. Acetone is often used to dissolve the glue, with a very unpleasant/painful sensation for the subject due to skin irritation and even skin breaching which occurred during the EEG-monitoring. During EEG-monitoring, inevitable gel drying requires regular refilling of the cap-electrodes, and displacement of electrodes during movement and sleeping is common, hence repositioning the electrodes by gluing is needed. Some doctors prefer the use of a tight cap combined with cup electrodes, to avoid electrode gluing. But for long term measurements, the thick cap is very unpleasant to wear, and heavy perspiration under the cap is often a consequence, causing severe itching and skin irritation. For long term home-monitoring of EEG, all wet-gel based systems are to be avoided due to the need of very regular checks/adjustments of medical trained personnel.

As an alternative, dry electrodes attract a lot of attention last years. Dry electrodes do not use wet gel, hence all gel-related disadvantages are overcome. Two groups of dry electrodes are investigated:

- Resistance-based dry electrodes, being conductive electrodes in direct contact with the skin. A low skin-electrode conductivity is aimed for. Such electrodes are also called direct-contact or Ohmic electrodes.
- Capacitive coupled dry electrodes, consisting of a conductive element covered with an insulator which is placed on the skin. A constant capacity is aimed for. Such electrodes are also called non-contact or capacitive electrodes.

Typically, dry electrodes for EEG are mounted in a headset (EEG) or they are kept in place by using elastic bands (EEG, ECG). For both electrodes it is important that the impedance, being resistive or capacitive, is constant, since varying impedance values will result in a faulty variation of the recorded signal. Therefore, obtaining good and stable skin contact is crucial, which is especially difficult when the subject is moving a lot (eg. during sports). The faulty signal variations related to movement of the electrode over the skin is called motion artifacts. Reduction of such motion artifacts by good electrode-skin adherence is crucial, and is still a real challenge for the EEG/ECG-system developers. Luckily, not only a constant skin impedance will reduce motion artifact problems. Also the electronics recording the signals can be optimized for motion artifact reduction, as well as the software dealing with the biopotential signals. Since doctors want always more representative ECG/EEG recording during normal life (instead of recordings while the patient is laying down in a hospital bed), motion artifact reduction remains one of the most important difficulties to overcome when using both types of dry electrodes.

Direct-contact Ohmic dry electrodes

Various types of Ohmic dry electrodes exist (Figure 3.2), some types are even commercial available such as the Sahara-electrodes from G-tec. These electrodes consist of gold-coated metal pins and the set-up time of this EEG system is very short. The elastic cap presses the low-impedance electrodes firmly to the skin, resulting high quality EEG signals, but the hard electrode pins become painful after long time recording. Electrodes provided by Quasar (see Figure 3.2) are having metal pins on a platform with a spring function in order to soften the skin pressure. The total construction is rather bulky, resulting in a lower amount of EEG signals to be recorded (lower resolution), and sleeping is certainly not possible with this system. The EEG-set is currently tested, in order to learn more about its properties/disadvantages, and further improve the system. The Mindo system releases pressure on the skin by providing a small spring in each electrode pin. Also this system is under test in order to improve it further. The systems listed above are a few of the many

EEG systems currently under development, using metal dry electrodes and dedicated solutions to realize good skin contact in order to reduce motion artifact.

Figure 3.2 :Some Ohmic dry electrodes and corresponding EEG recording systems for research use (a) from Mindo and (b) from Quasar; and commercial available so called 'Sahara' dry electrodes from G-tec.

Another approach is the use of conductive rubber electrodes (Figure 3.3). Such electrodes make use of the built-in elastic properties of the rubber to improve skin contact, without the unpleasant/painful pressure on the scalp during longer biopotential monitoring. Local non-flatness of the skin is elegantly dealt with. Since the impedance of conductive rubber electrodes is always higher than that of metal electrodes, the rubber electrodes can be used to measure ECG and EMG signals, but the weaker EEG signals can't be recorded by a simple electrode. For EEG signals, the electrode has to be connected with a small buffer circuit, converting the so-called *passive* electrode in an *active* one. Imec is performing extensive research on this topic, with very promising results for EEG recording using passive rubber electrodes and for EEG monitoring using active rubber electrodes (more information can be found in [1][2]).

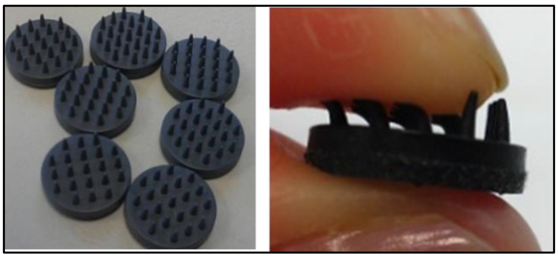

Figure 3.3: Conductive rubber electrodes for comfortable biopotential recordings without important signal quality loss.

It should be mentioned here that another type of Ohmic electrodes is investigated too, the so-called invasive direct-contact electrodes. Such electrodes are equipped with short and narrow microneedles, just sufficient to penetrate through the stratum corneum. In this way the skin layer with highest impedance is breached, and the physical attachment into the skin results in less motion artifact problems. Disadvantages are that skin penetration is always risky regarding pain and infection, eg. when locally the stratum corneum is thinner than expected. As a consequence, the material requirements regarding biocompatibility are rather demanding. Moreover, the microneedles are fragile structures, some needle breakage before or during skin penetration is expected. These disadvantages make the invasive Ohmic electrode less popular.

Non-contact capacitive dry electrodes

Capacitive electrodes will record a small signal only, even in case of the stronger ECG biopotentials. Hence designing an ultra-high input impedance amplifier (electrometer-grade with ultra-low noise level) is the main challenge in implementing non-contact electrodes. There are two key features in its design. First, it operated on charge displacement in the electrode (capacitance), not a transport of charge from the body to the electrode or vice versa. This eliminates the need to make direct electrical contact with the body. In its practical embodiment the probe can be positioned off the body at a distance of few mm, with a body-to-probe capacitance of few pF. Second, the high input impedance of the probe (a few times 10^{16} Ω at 1 Hz and an input capacitance in the order of 10^{17} F) ensured that the surface of the body, being the biopotential source, was not loaded down.

While the concept of non-contact biopotential sensors is not new, with the first working device reported decades ago, a practical ECG recording device for patient is now available. These probes will be truly non-invasive, drawing no real current, their coupling efficiency can be essentially perfect and they have a very much lower noise level than do conventional ECG sensors.

Electronic systems for wearable biopotential recording

The total wearable/portable biopotential monitoring system has also very strict requirements in terms of power dissipation, high signal quality, small area (minimal use of externals) and robust operation during ambulatory use. In addition, the need for for multimodal information acquisition requires even more functionality with minimal power dissipation. A very nice system [3] uses an instrumentation amplifier (IA) and achieves a fully integrated 200mHz High-Pass Filter (HPF) capable of rail-to-rail DC-offset rejection without compromising the CMRR (120dB) and is capable of actual real-time Motion-Artifact (MA) suppression before the ADC. This feature helps increasing system robustness during ambulatory use. Finally, a configurable ADC resolution and support for external sensors such as accelerometers and temperature sensors further enable multi-modal information acquisition for a consumption of 160μA.

Challenges for biopotential measurement systems

With regard to electrode technology, further development of the dry electrode based sensors is essential, since the higher user comfort and potential for independent home-use of such sensors is increasingly important. For both types of dry sensors, motion artifact reduction is important. Hardware, electronics and algorithms still need optimization towards optimal performance of such dry electrodes in combination with high user comfort and easy device handling. Regarding electrode hardware, miniaturization of the electrode and introducing mechanical flexibility is important. Ohmic dry electrodes can be used in a passive way for ECG, but for smaller biopotentials an active electrode is essential. For capacitive electrodes, active electrodes are always required, question remains if the smallest EEG signals can be recorded even with active capacitive electrodes. Integration of the electrodes into a comfortable elastic band/ cap/ headset still needs attention. Current systems are often unpractical, bulky, uncomfortable, impossible to sleep with, etc. Also the pressure of the electrode on the skin should be realized such that skin irritation/pain is avoided.

Regarding the systems electronics, more development is needed regarding motion artifact reduction and improvement of signal to noise ratio. Since wearable systems need to be small, ultra-low-power electronics are essential to avoid bulky batteries, which is in contrast to the higher demands on signal quality and multifunction-sensor systems.

In order to obtain a low-cost unobtrusive and widely acceptable device for electrophysiological health-monitoring (in particular for ECG applications) few problem are addressed by the research community. First, it's clear that the body surface and firstly the chest surface is only locally flat, a conformable/flexible or stretchable system will allow direct epidermal electrical measurement. Sensing interface has to be minimally invasive, conformable to human body and easy to wear, the recent developments of new sensing cloths that allow the recording of physiological signals demonstrate the potential of such approach.

The innovation in term of textile is related to the use of functional yarns integrated in the fabric for sensing and acquisition of vital signs. In this kind of design, electrodes and connections are all integrated in the material, the remaining electronics board use traditional technology. (see also section 5.5.4)

A more appealing system will take advantage of the recent development of printed electronics, a very robust and flexible patch based and printed electrodes and a mix between thin integrated circuit (for low noise Analogue Front End and other demanding functions) and printed electronics can be envisioned.

The ultimate goal in terms of wearable health monitoring device would be a temporary film tattoo with embedded electrodes and electronics, battery or energy harvesting system that can endure repetitive mechanical deformation on skin body surface and wirelessly transmit signal to a smart-phone like base system.

3.2.2 Implantable electro-physiological sensors

State of the art

Many applications such as treatment for spinal cord injury, cochlea implants, retinal prosthesis, epilepsy, Parkinson disease, depression, cardiac dysrhythmia, obesity, the drop foot stimulator, sensory deficits … can potentially benefit from the application of electro physiological technology. In past decades, many different approaches have been considered for contacting nerves, muscles or brain. The electrodes are a critical element for establishing the electrical connection to measure the neural activity and to stimulate the neurons the muscles for controlling the organs, the limbs or for overcoming the sensory deficits.

A neurostimulator is a device designed to stimulate generally deep brain structures such as the thalamus, the sub-thalamic nucleus or the globus pallidus. This cerebral implant can be done in each hemisphere for bilateral troubles. Stimulated zones can vary depending on the indication, as the size of the zone to stimulate can vary greatly (e.g. as big as a rice grain for the subthalamic nucleus, a.k.a. STN).This sort of electrotherapy can be used to treat Parkinson's, shakes, obsessive-compulsive disorders and dystonias.

Deep brain stimulation [4] was designed by Professor Alim-Louis Benabid and his team from CHU Grenoble in the 80s. This mode of stimulation is also called high-frequency brain stimulation, but DBS is the commonly-used acronym. The largest use for this sort of therapy is to treat patients with Parkinson's, and Professor Benabid revolutionized this field by designing a treatment for patients whose condition was unresponsive to classical pharmacological treatments.

A vagal vagus nerve stimulator is an implant placed under the patient's skin, like brain stimulators, and meant to generate pulses to excite the vagus or pneumogastric nerve

(Vagus Nerve Stimulation, VNS). Although controversial, this method is used to treat epileptic patients and for some pharmaceutical-resistant depressions.

Over 25000 patients worldwide suffer from urinal (miction problem) or fecal incontinence already benefit from such a device. Its therapeutic vocation is the neuromodulation of the sacral nerves (or sacral roots), designated by SNS (Sacral Nerve Stimulation). The relevant nervous structures are concentrated in the lower back (just above the coccyx). This electrical stimulation aims to eliminate or reduce some symptoms of incontinence. Chronic pain management is one of the great challenges of medicine. Over time, pain can overshadow all other aspects of life and the people afflicted can suffer for no reason for years. When pain doesn't respond to classical therapy, spine stimulation can be offered. With some patients, this stimulation can help them overcome chronic pain and allow them to return to a more active lifestyle.

The trend for these types of stimulator and other peripheral nerve stimulation is to mix stimulation and recording. This implies the careful design of implantable micro-electrode and high performances ultra-low noise analog front end stage. The ultimate gold of the recording function is to allow a real closed loop system for an optimum stimulation control. But the main field that involve implantable electro-physiological recording pertains to the domain of Brain Computer or Brain Machine Interface as discussed as follows.

Reliable and robust brain machine interfaces (BMI) that enable direct patient control of motor prosthetics are an ongoing challenge. Electrophysiological methods to communicate and probe the nervous system have been explored extensively. Implantable probes with single or arrays of neural recording and stimulation electrodes, simply referred to sometimes as ''neural probes'', that reliably interact and communicate with neurons have served as standard neuroscience research tools for studies of brain function for decades but have yet to achieve their potential in clinical use.

Individuals with neurodegenerative disorders or other neurological deficits may benefit from neural probe technologies to restore brain function lost by disease (stimulating electrodes) or re-establish previously severed brain-limb connections as in limb control (recording electrodes).

Earlier BMI technology consisted of individual metal microwires (0.75 mm diameter) with de-insulated tips for recording neural signals. Later, arrays of microwires held together with adhesive led to improved spatiotemporal neural recordings. With the emergence of microfabrication technologies, silicon (Si) shanks supporting patterned microelectrodes were developed for use as neural probes; today, two probe types are prevalent. The Michigan probes, introduced in 1986, consist of Si micromachined probes with multiple electrode recording sites patterned along the shank (later commercialized by NeuroNexus). The Utah probe array, introduced shortly thereafter, consists of arrays of Si micromachined shanks each with an individual metal recording site located at the shank tip (later commercialized by Blackrock Microsystems). Dense arrays of recording sites are possible with either technology platform.

Despite many decades of development, reliable neural recordings are typically obtained in durations measured in months. This short lifetime is attributed to the physiological response of surrounding neural tissue to the implanted neural probe. Upon implantation, brain micromotion due to blood flow, respiration, and head movement aggravates the tissue surrounding the device and a physiological response begins that involves inflammation, glial scar encapsulation of implant, and retraction of neurons from recording sites leading to a loss of recordable neural signal. One contributing factor for tissue aggravation is the mechanical mismatch in elastic moduli between the stiff probe material and surrounding soft neural tissue.

Microwires made of noble metals or micromachined Si shanks (Young's modulus, Ey 100–400 GPa) possess Young's moduli many orders higher than neural tissue (Ey 0.1–6 kPa). A neural probe technology which has achieved long recording lifetime (in both animals and humans) measured in years is the neurotrophic cone electrode.

To overcome manufacturing and electrode density limitations of cone electrodes that prevent its widespread use, a batch fabricated Parylene flexible neural probe using a novel process that enables a three dimensional (3D) sheath structure was developed [5]. First, surface micromachining techniques are used to define the initially flat Parylene neural probe structure. A post-fabrication thermoforming process is used to obtain the final 3D structure and open the lumen of the sheet.

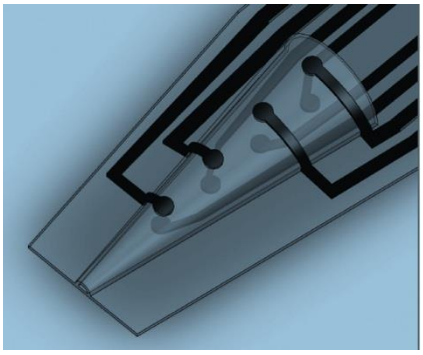

Figure 3.4 : Parylene neural probe with 3D shealth

For recording and stimulating, the cuff electrodes (a tube surrounding the nerve over some length) provide a suitable interface for the peripheral nervous system, hence the need of conformable electrode. As explained previously, the mechanical mismatch between the silicon rigidity and soft neural tissue was an issue, consequently the scientific community has developed more flexible probes. Previously, silicon has been the most commonly used substrate material. Some research groups have focused on flexible electrodes based on MEMS technology, for a less invasive approach. The most popular polymers are: polyimide [6], parylene [7], SU8 [8], Avatrel/polynorbornene[9], silicone[10], liquid crystal polymer [11].

A wide range of materials has been used for active area, including stainless steel, tungsten, platinum, and platinum-iridium alloys, gold. To record or stimulate the neural activity, the electrodes need to have high selectivity and sensitivity. For increasing the selectivity, i.e. the ability to activate the target neural tissue, without activating surrounding population, the active surface decreases for improving the spatial resolution. Unfortunately, smaller size of an active area increases the electrode impedance, which can degrade the sensitivity. There is a trade-off between the selectivity and the sensitivity.

To address these limitations, many electrode materials with higher injection charge and lower impedance have been evaluated. The most popular ones are Iridium oxide [12], platinum, carbon nanotubes [13], [14], poly(ethylenedioxythiophene) (PEDOT) [15], diamond [16], titanium.

The packaging of the flexible microelectrodes is challenging, particularly with respect to wire bonding. For the fabrication of multichannel electrodes, multiple wires must be connected to thin and small electrodes. Several packaging techniques have been reported: Zero insertion force [17], the stud bump acts as rivet [18], the ACF (Anisotropic

Conductive Films [19], commercial connector (Omnetic for example [20]) attached with conductive epoxy [21] . As the number of interconnections increases, the individual wires are replaced by flat flexible cables (FFC). The ribbon cables are conformable, and allow a collective approach for the electrical packaging.

Recently, some research centres developed neural probes with sensing sites and fluidic channels [22]. Stieglitz's team fabricated sensing electrodes which can conduct light as well fluids .Organic electronic appears as a promising add-on for the in-vivo recording, because of their flexibility and their biocompatibility[23]. A local amplification of the recording signal is very interesting, for improving the signal-to- noise ratio [24].

3.2.3 Trends

The Obama administration is planning a decade-long scientific effort to examine the working of the human brain and build a comprehensive map of its activity (project called "Brain Activity Map"). Scientists with the highest hopes for the project also see it as a way to develop the technology essential to understanding diseases like Alzheimer's and Parkinson's, as well as to find new therapies for a variety of mental illnesses.

The trend in neural prostheses and electrical stimulation is towards system having a higher density of electrodes: especially for recording the neural activity (the brain is roughly 100 billion neurons, currently only a small number of neurons are measured at once), for high spatial resolution for retinal stimulation, for focal stimulation of nerve ….

An important advantage of the microelectrode is the ability to stimulate a comparatively small volume of neural tissue and to record the action potential from small population of neurons. Increasing the number of electrodes improves the spatial resolution and the selectivity.

The development of higher density for MEA has to face several aspects:

- The technology requires more sophisticated integration, with several metal layers with via technology, for ensuring the routing of metal lines.
- Smaller electrode surface requires material with high injection charge capacity, or develop the surface area by structuring the active surface (roughness, micro structuration).
- A good signal-to-noise ratio is a key factor for recording. Smaller active area induces higher impedance, consequently affects the noise. New materials have been studied for decreasing the impedance.
- Micro wire spatial requirements for connecting the MEA is the limiting factor for the miniaturization of the electrode size. Collective and flexible packaging solutions have been investigated. The multiplexing especially for the brain is one of option for electrical connection the contemplated. The optical connection for retinal implant has been also considered.

Hybrid interface are developed for interconnecting the microelectrode and electronics for an enhanced functionality and an improved biocompability. Flexible electronics have shown significant progress. An electronic nearby the microelectrodes provides new possibilities for conditioning the neural signal: multiplexing, amplification …

The development of electronic with very low noise and with low current consumption is critical for an implantable device which process signal at very low voltage (μV). The objective is to obtain adaptive prostheses that modulate stimulation in response to recorded neural signal.

Progress has been made in the development of hybrid/ rigid probes for depth recording for the brain for example, for reducing the inflammatory response. Sheath flexible electrodes are developed; the insertion is performed with an introducer tool, or with an integrated rigid material which quickly dissolves. Currently, 3D probes with sensing sites and fluidic channels have been reported.

New therapies are investigated with the vagus nerve stimulation, also for neurological disorders with light stimulation (optogenetics).

Several companies have been developing new generation for the pacemaker: the leadless pacemaker, which can be directly implanted into the heart (Medtronics, Sorin) and includes an energy source (rechargeable battery and/or energy harvesters, all in the same miniaturized microsystem). The overall complete system is ultra-miniaturized and exploits the heterogeneous integration of high density submicron technology chips, RF transmission, low leakage high density battery and/or energy harvesters with a power management electronics, in a volume of the order of few cm^3.

3.2.4 Future development

In the clinical practice, the current neural prostheses dispose of a low number of electrodes. But their low degree of miniaturization and the poor resolution limits their applications. The tendency is toward systems having high number of electrode channels that each provides localized stimulation and recording. The strict anatomical constraints (for example for retinal implant) require achieving smaller and thinner medical devices. To reach these goals, the development of technology with multiple metal levels to make denser routing is necessary.

The evolution of MEA has arrived at a level where packaging restricts the achievable performance of the final device. The packaging of the electrodes with high number of active area requires elaborating a reliable collective and flexible solution. As the pitch size decreases, reliable fabrication of interconnections is more challenging.

The size of multiple wirings is a limiting factor to increase the number of electrodes. Novel solutions have to be contemplated: multiplexing, optical control with asynchronous camera, hybrid interface… The signal processing is a key component when the number of sensors or active area increases drastically.

The development of smarter prostheses that modulate or initiate electrical stimulation or the drug delivery, in response to recorded neural signals or chemical sensors is also considered. Research centres will have to elaborate solutions to fabricate multimodal electrodes: with sensors, drug delivery or/ and light transmission. The adaptive prostheses require a signal processing appropriated for onboard electronic: i.e. with a low complexity for ensuring a small current consumption and a fast response. Consequently, a new generation of microprocessor and associated electronics will have to be elaborated for meeting the requirements of a very low noise, highly efficient components, and a low temperature rise.

Electrode materials have been identified and selected for their in vitro electrochemical properties relevant to stimulation and recording. Nevertheless, chronic implantation shows that electrode properties often changes over time. The explanations for the variations are not clearly established: evolution in the tissue encapsulating the electrode, modification of electrode materials, or a difference in the response of the neural tissue. Investigations will have to be run to identify the factors. The closed loop of the medical system will have to include the measurement of the quality control of the electrodes (a nondestructive method has to be identified).

Techniques need to be developed to maintain the low impedance of the sensing electrodes over time. A recent and potentially important approach to improving the performance and stability of microelectrodes is the use of biologically inspired electrode treatment. The promising enhancements of the flexible electronics offer tremendous opportunities for the neural prostheses: especially for the signal conditioning. The development of the association of the MEA with flexible electronics is one of the key to extend the functionality, and also to mitigate inflammatory and encapsulation processes in the surrounding tissue.

For the leadless pacemaker and more generally for the neural prostheses, the development of ultra-miniature electronics have to include: high density submicron technology chips, the RF transmission, low leakage high density battery, … . The size of the battery is a limiting factor for miniaturization of medical device. The development of new generation of smaller very high density battery or of transcutaneous battery recharging system should reduce the volume of this component.

3.3 Inertial MEMS sensors for human activity

Recently, we have experienced a very rapid adoption of inertial sensor technology into many consumer electronics products, with the smart phones, tablets, gaming systems, driving very large booming markets. Another driving force of this adoption was the reduction in cost per sensing axis enabled by highly integrated silicon micro electromechanical system (MEMS) with complementary metal oxide semiconductor (CMOS) technologies. It is worth noting that such multi-axis sensors of multiple types now coexist on a single silicon substrate and in a small low-cost plastic package. For example, 6-axis sensors integrating 3-axis gyroscopes with 3-axis accelerometers are becoming ubiquitous in smart phones. MEMS-based detection of motion is becoming a leading technology for inertial sensors allowing full integration with silicon circuitry of individual sensor and even the combination of three major sensors categories: accelerometer, gyroscope, and compass that are now defining standards for motion sensing in most smart phones and tablets. Their use in smart phone applications has also bring high on the agenda the requirements of low power consumption, making these devices suited for current and future wearable systems applications in health and wellbeing.

3.3.1 State-of-the-art of MEMS inertial technology

In any inertial system, a proof mass, m, is suspended on a mechanical frame by a spring, k_m, and responds to an input force, F, mirroring a quantity to be measured. The input force causes a displacement, x, of the mass, and the displacement is measured to sense the force. This input force may come from: (i) acceleration of the mass, as is the case in an accelerometers or from a Coriolis acceleration, resulting from angular rotation of the mass, as is the case in a vibratory rate gyroscope. These inertial sensors can have different transduction mechanisms: charge transduction, force transduction and electrostatic spring constant. Design optimization of inertial sensors aims at high transduction gain, while rejecting the effects of parasitic forces on the mass. The inertial MEMS sensors require analog/mixed-signal circuitry to process and digitize the sensor output. Sensor interfaces supply a stable voltage bias to the MEMS device, amplify the flow of signal charge to a measurable level while maximizing signal-to-noise ratio (SNR) and provide the necessary signal processing to filter and extract the desired signal. On top of these figures, the sensor performance stabilization over a temperature range imposed by applications (for instance: -40°C to +105°C) is required.

Important aspects for the wearability potential of such sensor are the *low power consumption* and the *small size* of the inertial sensors. The energy efficiency of inertial sensors is currently evaluated by some specific figures of merit. In his recent review article, D. Schaeffer from InvenSense mentions that such useful energy-based figure of merit (FOM) is a power ratio) of peak SNR to energy per conversion. A higher FOM indicates a more energy efficient sensor operable at lower power consumption for a given noise performance or, alternatively, having lower-noise operation for the same power consumption. Energy (or power) constraint design can become in the future a more stringent demand for self-powered wearable systems, also imposing difficult constraints on resolution and SNR.

The state-of-the-art in MEMS for inertial measurement is dominated by the progress made by some industrial manufacturers like ST Microelectronics, Texas Instruments and InvenSense. For instance the ST Microelectronics include analog and digital accelerometer and gyroscope sensors with advanced power saving features (such as low power mode, auto wake-up function and a FIFO buffer that can be used to store data, in case of their accelerometers) that make them suitable for ultra-low-power applications. The ultra small size (including advanced packaging) and the embedded features of ST's accelerometers and gyrsocopes make them an ideal choice for handheld portable applications where there are stringent requirements for long term operation. STMicorelectronics is currently the world leader in the market of MEMS inertial sensors having delivered more than 3 Billions MEMS units and with a manufacturing capacity in 2013 larger than 3 million units per day (based on two manufacturing sources).

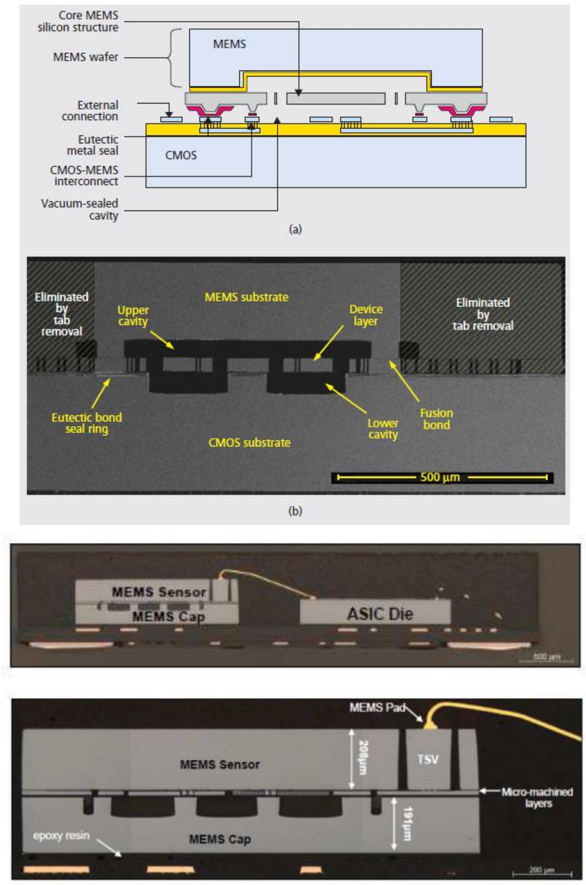

Figure 3.5 Left: InvenSense silicon MEMS/CMOS fabrication technology: a) assembly; b) device cross-section and Right: ST Microelectronics Thru-silicon.via integration of MEMS sensors for highly compact and robust inertial sensing. Source: Benedetto Vigna, ST Microelectronics.

Trends

The trends in inertial sensors for human physical activities are dominated by the industry push to integrate silicon MEMS/CMOS technology multiple sensor functions onto a single die with compatibility with low-cost plastic packaging and therefore reduce the cost per functions. MEMS-based inertial sensors seem to dominate this market offering miniaturization and low cost in large volumes.

An increased interest in the energy-based figure of merit is observed because of the use of many inertial sensors in smart portable applications, which also triggers the exploration fundamental performance tradeoffs and provides a framework to quantify and compare the performance of different sensors. The accelerometers and gyroscopes (3-axis Digital Accelerometer, 3-axis Digital Gyroscope, announced by STMicorelectronics in 2013), with their readout interfaces are the key sensors for the inertial sensing but also pressure sensors and compasses (6-axis Digital e-Compass:) became part of the portfolio of manufacturing companies of MEMS inertial sensors.

Future developments and challenges

Inertial sensor level

Recent trends deal with the exploitation of further miniaturization by using the Silicon-on-Insulator technology for even smaller in size and power consumption *Nano-Electro-Mechanical-Systems (NEMS) accelerometers*. NEMS seems promising for ultimate sensing, autonomous sensors, battery-operated systems and can allow new architectures. The SOI CMOS technology developed by CEA-LETI allows the integration of NEMS accelerometers in the front-end, therefore combining the CMOS circuitry and the NEMS devices in an even more compact way. However, the use of NEMS raise important problem to the capacitive detection schemes and their integration because extremely small variation of a capacitance has to be detected with low power consumption and reasonable SNR. These issues are being solved today by the use of new integrated detection schemes like piezoresistive [25] or FET active detection with channel charge modulation [26]. These solutions have the advantage of being more compact and reducing the requirement on the sensor readout that can be simplified because it deals with current variations insated of ultra-small capacitance variation. Moreover, the full compatibility with SOI CMOS front-end ensures the integration of the sensor and circuitry with reduced parasitic and enables the use of thin film packaging techniques at wafer level. Tronics recently launched a new large-scale project to industrialize CEA-Leti's breakthrough M&NEMS (Micro and Nano Electro-Mechanical Systems) technolog based on piezoresistive nanowires rather than pure capacitive detection, which is now on market.

System and application level

One of the clear and important trends is about *offering full integrated solutions* for inertial sensing, including the inertial sensors (accelerometrs and/or gyroscopes), the MCU, the software fusion and the power management. Companies like ST Microelectronics offer full platforms with access to software for customer development dedicated solutions. This is an important advantage for the take-up of inertial sensors in smart systems for healthcare and well ness, both for evaluating the activity of the elderly or the performance of athletes based on the same platform that can be personalized depending on the application.

3.4 Bio-chemical sensors

Nowadays, the use of wearable sensors to monitor various health related biometric parameters during daily activities is attracting increasing interest. Many people are familiar with the use of devices such as wearable heart rate monitors and pedometers for medical reasons or as part of a fitness regime. Interest in the use of such wearable systems for personal health and rehabilitation has grown as part of a wider initiative to increase the input of the individual or patient in their own care. It is thought that this may assist in reducing the strain put on healthcare systems by ageing populations, rising costs and an increase in the incidence of chronic diseases requiring long term care. To date the focus has been on the use of wearable sensors to convert physical biometrics such as heart or respiration rate into electrical signals. For example, EU funded projects have used sensorised cotton/lycra shirts to measure respiratory activity, electrocardiogram (ECG), electromyogram (EMG) and body posture. Other systems include the Lifeshirt®, developed by Vivometrics®, the body monitoring system developed by BodyMedia® and the well-known Nike-Apple iPod Sports kit.

Despite the growing success of sensors which monitor physical properties, relatively little has been done in the area of wearable chemical sensors which can be used for the real-time ambulatory monitoring of bodily fluids such as tears, sweat, urine and blood. Some great expectations were driven by wearable systems for monitoring sugar levels in diabetics like the GlucoWatch Biographer, but now GlucoWatch has vanished from the diabetes care scene and its manufacturer has stopped any further development.

The widespread use of chemical sensors has been complicated by several factors which are difficult to overcome. These include sample generation, collection and delivery, sensor calibration, wearability and safety issues.

It is estimated that 70% of all illnesses are preventable resulting in increased costs for treatments and medication. Many of these illnesses could be prevented by adopting suitable diet and partaking in regular exercise. Exercise generates sweat naturally, and sweat contains very rich information about the physiological condition of the subject as it contains a matrix of essential ions and molecules. Sweat analysis is known to be used to identify pathological disorders such as cystic fibrosis, which implies its potential as an important diagnostic tool for other disorders when suitable markers are identified. On the other hand, real-time sweat analysis during exercise can give valuable information on dehydration or heat stroke and changes in the concentration of important biomolecules and ions. This information is very important for monitoring the subject's physiological conditions during training/exercise and can be used to determine suitable approaches to rehydration and re-mineralisation or to elaborate new strategies of exercises. In the case of people who enjoy endurance sports, it is well known that sweat composition changes during exercise as a result of dehydration. A 2% drop on body mass due to fluid loss can have a serious effect on performance and further losses may lead to symptoms such as irritability, headache, dizziness, cramps, vomiting, increased body temperature and heart rate, increased perceived work rate, reduced mental function, slower gastric emptying. Alternatively, drinking too much can lead to hyponatremia or low levels of sodium. This results in headache, nausea, muscle cramp and vomiting. If the onset of this condition occurs over a short period of time, for example during exercise, it can lead to more severe complications such as seizures, coma, brain damage and death. Therefore, constant monitoring of the composition of sweat can lead to tailored rehydration strategies which improve performance and preserve the health of the athlete. As exercising in a dehydrated condition has been shown to lead to increased levels of $Na+$. Furthermore, it has been reported that sweat pH will rise in response to an increased sweat rate. A relationship was also observed between pH and sodium ($Na+$) levels in isolated sweat glands in that the greater the concentration of $Na+$, the higher the sweat pH will be. As exercising in a dehydrated condition has been shown to lead to increased levels of $Na+$, it can be seen that such changes can be measured directly (using a Na+ selective sensor) or indirectly by monitoring the pH of sweat

State of the art

In the field of sweat analysis, the design of a textile based fluid handling system and pH sensor based on paired emitter-detector LEDs has been demonstrated in the work of D. Morris et al [27]. The designed fluid handling system was able to collect sweat from the skin and transport it in a controlled way down the channel and into the absorbent during in vitro and in vivo trials. Furthermore.an On-fabric pH sensor was developed immobilising a pH sensitive reagent directly onto a textile material which will give a visible colour change with variation of sweat pH. The results are shown in Figure 3.6. The sensor exhibited a colour change from yellow to blue in the region pH 4–7 which was detected by the optical detector.

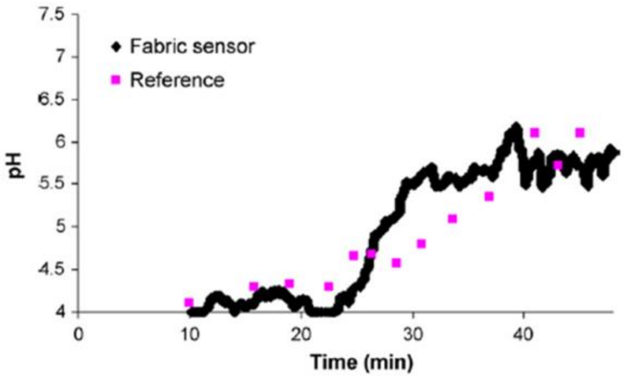

Figure 3.6: pH values recorded during on-body trial.

Measuring ion concentrations directly in bodily fluids such as sweat, inherently gives information on both electrolyte volume and concentrations in plasma, and serves to indicate if these are in order. However, this approach is limited largely due to the unavailability of in situ and/or real-time electrolyte measurement devices and methods. Sweat monitoring and analysis in a convenient and in situ manner could play a major role in facilitating accurate and timely control of hydration, and therefore enhance performance. Electrolyte levels in sweat including Na+ levels vary considerably depending on the point of the body where they are measured. Additionally, Na+ concentration varies widely depending on genetic predisposition, diet and heat acclimatization rate. Conversely, sex and aging do not appear to have a large effect on sweat electrolyte concentrations and no definitive correlation is apparent. Interestingly, dietary salt intake and sweat rate also do not specifically correlate to sweat electrolyte concentrations. These factors underline the individual nature of absolute sweat electrolyte concentrations, and coupled with exercise induced changes over a narrow timescale, make sweat concentrations difficult to interpret, due to the multitude of factors that could be influencing the observed values.

Clinical interest in sweat electrolyte analysis includes the diagnosis of Cystic Fibrosis (CF), indicated by abnormally high sodium levels in sweat. In CF diagnosis, specific sweat electrolyte concentrations (usually Na+or Cl−) are determined in a technically complex manner that is not in realtime. Because a specific concentration threshold is available and a small number of analyses are needed for confirming CF in each patient, accuracy is of singular importance – already provided by existing methods of analysis. However, in the area of treatment (e.g. rehabilitative physical exercise for CF patients) and monitoring, high frequency real-time sweat electrolyte data would again be useful.

The work of B. Schazmann et al., [28] tackle this problem by designing a wearable system based on ISE (Ion Sensitive Electrode) technology for the sodium dosage. Although compact solid state technology was used, the sodium data (ISE based) exhibited non-Nernstian slopes, severe drift and poor reproducibility. This is attributed to the fact that solid-state ISEs in the form used were inherently less stable (both working and reference electrodes) than their classic inner solution based counterparts. A large number of cations and anions can be selectively analysed according to the many ionophores available for use in ISEs.

The integration of an Ionic Selective Electrode (ISE) sensor on fabric able to detect and quantify selectively Na+ ions in natural sweat and the development of a portable electronic board connected to the sensing part driving several ISEs and temperature sensors and converting electrical measurement data to ions concentration is presented in a paper of G. Marchand et al. [29]. The developed electrochemical sensor consists of host molecule included in a conducting polymer, to perform specific transducer that precisely and selectively measures the sodium concentration. Thus, the complexation of the targeted ion (with positive charges) by the host molecule leads to a modification of the electrochemical response of the sensing part. This modification is measured by the evolution of the open circuit potential (OCP). an electrochemical sensor, specific of Na+ ions, was developed and transferred on fabrics. A dedicated portable electronic board was also developed to drive the sensing part and to convert the electrical signals to ions concentrations. The complete system was successfully validated with natural sweat.

The intrinsic design of conventional ion-selective sensors imposes inherent limitations upon specific ex vivo applications; particularly the internal solution complicates the fabrication process and limits their miniaturization. Furthermore, traditional ISEs are often fabricated by employing rigid materials which hinder their integration on not flat surfaces. The work of Amay J. Bandokvar and al. [30]. reports on the development and characterization of ion-selective potentiometric electrodes fabricated on temporary-transfer tattoo paper for direct epidermal pH measurement. The new fabrication route yields highly flexible body-worn potentiometric sensors that area compliant with the skin.

Challenges

It was found that standard dielectric materials normally employed in microelectronics technology can be used in making ion-sensitive field-effect transistors and ion-selective microelectrodes for biosensing applications. The future challenge is to properly integrate all the components (polymer membrane, biochemical compound and micro-electrodes) of the biosensor coupled with the electronics circuits in a robust and practical manner and to validate in real conditions the functions. Furthermore, a diversification of the sensors could be evaluated in order to target relevant small molecules such as lactates, urea, glucose etc. The next step would be the packaging and assembly of the sensor on a flexible substrate bearing printed electronics high performances circuits with embedded processing power and wireless functions.

3.5 Sensors for gas and airborne particles

Our environment, whether outdoors or inside the buildings in which we are living or work, impacts our health and our lives directly through the air we breathe. Many potentially harmful factors cannot be noticed by humans at all; there are no human biological sensors for pollutants created by our industrialized world, since evolution is too slow to catch up. So artificial “sixth senses” are needed to assist our biological ones. These sensing devices will stand at the interface between people and their environment, providing relevant and real-time information, acting as personal assistants to guide, enable, and protect us all, and to make our lives more enjoyable as a result. In addition to analysing the air we breathe in, there is also great interest in analysing the air that is exhaled. Since our breath reflects our health status, its composition can be utilised as an early indicator of potential health issues.

Being able to measure the concentration or presence of airborne factors is the core function of “sixth sense” devices that perform ambient air or breath analysis. For air quality monitoring, many organizations including the European Commission [31] and United States Environmental Protection Agency (EPA) [32] have define clear indoors and outdoors air quality standards for gases (NO_x, SO_2, CO, O_3, C_6H_6, CH_2O, VOCs), toxic metals (Pb, As, Cd, Ni, Rn), inorganic particles (PM2.5 and PM10), and identified over 187 toxic air pollutants [33]. To these one may add other organic airborne factors of great potential health impact such as pollen, microbes, viruses, and spores. Health effects for the above listed factors vary greatly depending on the exposure dose and time, but they may range from mild eye, nose and throat irritations to severe immunological, neurological, reproductive, developmental, and respiratory problems and increased risk of cancers.

State of the art

Airborne factor analysis can be currently performed in dedicated facilities, based on specialized, costly instrumentation. A portable, energy efficient solution for air analytics has the potential to revolutionize the way we sense and understand out environment. Despite its importance, such a solution is still missing.

Focusing on energy efficiency and portability, the most promising gas sensing principles include chemiresistors (semiconducting metal oxides, polymers, and functionalized nanowires), chemicapacitors, chemtransistors (ISFETs, ChemFETs, SGFETs), mechanical structures (QCM, SAW, MEMS and NEMS) and calorimetric sensors. Despite their superior resolution, optical transducers are power-hungry and bulky, their usefulness being thus confined to applications where sampling rates ~10 mHz (1/min.) and below are acceptable. Electrochemical transducers with solid electrolytes are very difficult to miniaturize despite their intrinsic selectivity and low power consumption. Several textbooks and articles review the different types of chemical sensors [34][35], their operation and application scenarios.

Regardless of their transduction principle, most gas sensors employ a sensitive layer, whose role is to tune sensitivity and selectivity. Each pair of sensitive-layer/target analyte exhibits a maximum in the sensitivity versus temperature characteristic, reflecting a broad distribution of reaction-diffusion rates and interactions. For example, polymers typically require 30-60°C whereas metal oxides are typically operated at elevated temperatures 200-400°C, although room temperature responses to O2 and CO using very thin films and catalytic surface particles have been reported recently [36]. Integrated heaters can quickly (~10 ms) and efficiently raise the temperature of a gas sensor, but they still require around 5-20 mW to reach 400°C [37][38][39]. For example, Figaro Engineering offers a variety of metal oxide sensors such as TGS2442 for CO, NH_3, H_2S, and TGS2620 for organic solvents that require at least ~14 mW for the heater. On the other hand, the small heating-cooling time constants provided by micro-hotplates, have enabled temperature modulation techniques (transient or cyclic) as a strategy for improving selectivity [40][41][42], at the expense of slightly increased sampling rates. The ultimate miniaturisation of heated gas sensors is perhaps represented by self-heated suspended nanowires [43][44] for which a power consumption as low as 20 μW (excluding readout electronics) has been reported [44]. Ambient temperature digital sensors from Micronas will be available soon for gases such as O_3, NO_x, CO, CO_2, VOCs, NH_3. Micronas’ GAS 85xyB sensor is based on CCFETs, and consumes ~30 μW.

Regarding airborne particle detection, most techniques involved in aerosol analysis utilize laboratory instrumentation such as mass spectrometry, optical spectroscopy and several other types of microscopes and analysers on off-line samples [45][46]. Recently, there have been some attempts to miniaturize particle detectors; in [47], a miniaturized MEMS particulate matter (PM) monitor consisting of an FBAR mass balance and two optical absorption (one IR and one UV) sensors, was shown to detect PM concentration as small as 18 $\mu g/m^3$ with a power consumption of <100 mW.

Challenges

The recurrent theme in all the applications involving airborne factor analysis is that many miniaturized and affordable sensing units are needed in a wirelessly-communicating mesh that can be autonomous over extended periods of time. For wearable sensors, zero-power technology is essential. But the same holds true for sensing in buildings: The current state-of-the-art is wired sensors (energy and data lines) with high cost due to installation effort, only affordable for industrial monitoring purposes like fire detection. Battery-based consumer devices lack communication functionality and run into problems with empty batteries. To bring the cost down to a level that allows widespread use in our private environment, with full functionality including networked communication, the reduction of installation cost is essential. In addition, the devices need to be self-sustaining over long periods of time (with no battery changing) to allow for proper wireless communication in a self-configuring manner. The same thing holds for the outdoor sensors that report on the status of the environment and communicate this information indoors. Ease and cost position of deployment are decisive in order to make such devices usable in our daily lives.

Most of the gas sensing technologies listed in the State of the Art paragraph above have the potential, if given due time and resources, to reach power consumption figures that would make them interesting for most of the targeted applications. For example, suspended, self-heated SnO_2 nanowires have been demonstrated for sub-ppm detection of NO_2 recently, with 20 µW of power consumption[43]. Energy harvesters can actually produce that much power. Indeed, the same group has demonstrated a fully autonomous gas sensor system based on self-heated SnO_2 nanowires that is powered from a thermoelectric microgenerator [48]. This demonstration barely shows the way, as other suspended, self-heated one dimensional nano-structures such as carbon nanotubes and various nanowires hold the potential to result in even further power consumption reduction [49]. Open challenges for these technologies are related to their lack of selectivity and insufficient characterisation with respect to environmental parameter variations such as humidity and other non-target analytes. A platform capable of distinguishing a set of the most important gases reliably in a realistic environment still remains to be demonstrated. Large scale fabrication technologies with acceptable yields are also waiting to be developed.

The situation for sensors particle and airborne pathogens is much more unclear. This field is virtually in its infancy with no commercial products available yet and only a few academic demonstrations. The MEMS particulate matter (PM) monitor mentioned in the State of the Art paragraph had a power consumption of <100 mW. Whereas this is too much for most energy harvesters to provide, one can argue that some of these sensors need to be operated only a few times a day and not continuously which would amount to a much lower average power consumption. In other applications however, such as airborne pathogen detection continuous sampling might be required, justifying the need for developing ultra-low power transducers.

3.6 Integrating electrode: Patch

State of the art

Microsystems hold an important place in new technology developments applied to analytical chemistry, biomedical, diagnostics or wellness for instance. Conventional microsystems are built on planar architecture based on silicon or polymer technology.

These last 10 years, much work has been performed to develop devices that adapt dynamically to curving and bending surfaces. Some examples include automotive, biomedical systems for diagnostics or wellness such wearable health monitors (e.g. electrocardiogram or temperature sensors). Part of bendable and foldable devices is made with the roll to roll technology. This technology is still in development and several groups around the world work on it and bring innovative devices into light. The VTT research centre in Finland and the HOLST centre in Netherlands have a roll to roll pilot line for instance. Among devices developed on soft materials, the Holst centre works on sm-OLED, MEM-OLED, memory and pressure touch transistors. The VTT research centre vision is to employ printing processes to create easy-to-use and cost-effective products for sensing, light-emitting surfaces, energy foils, optical films and electrical circuits. At the Fraunhofer institute, they merge MEMS technologies, for example, with microfabrication technologies on film to produce electrochemical sensors on film substrates. These sensors have a wide range of uses. They can determine the level of vitamin C in orange juice or detect explosives in airport.

As a complement to traditional silicon-based microelectronics, the CEA-Liten develops printed electronics based on organic materials to enable the manufacture of large conformable electronic components and to integrate active functions on flexible substrates in consumer products. The technologies developed comprises:

- Electronic components: resistors, capacitors, antenna
- Logic circuits, printed transistors (OTFT and CMOS)
- Interconnection and integration with manufactured products
- Sensors and sensor arrays: temperature, pressure, piezoelectric, photo diodes, OLED

CEA-Leti is also working on flexible devices for medical applications. Among the applications, there are smart band-aids enabling to monitor and evacuate the exudate from wounds. Another application concerns the wellness. It is the analysis of ions in sweat to monitor the dehydration of a person.

Imec announced in September 2012 [50] that it has integrated an ultra-thin, flexible chip with bendable and stretchable interconnects into a package that adapts to curvy surfaces. The device is an ultrathin polyimide microcontroller integrated with stretchable electrical wiring embedded in an elastomeric substrate, e.g. polydimethylsiloxane (PDMS).

In the last years innovative concepts more suitable for wearable or implantable systems like personal health monitoring or eye-type imagers emerged based on foldable and stretchable architecture. In 2011, D.H Kim et al. [51] presented in a Science paper a tattoo-like epidermal electronic system incorporating electrophysiological, temperature, and strain sensors, as well as transistors, light-emitting diodes, photodetectors, radio frequency inductors, capacitors, oscillators, and rectifying diodes.

For decades, extensive research was performed for the analysis of biological samples. Biological detections and diagnostics involve transferring, purifying, mixing fluid samples and analysing them. The samples need to be captured either from the environment, or directly on the skin or into the body. Following the development of foldable and stretchable electronics, emergence of microfluidics systems become complementary to expansion of foldable and stretchable electronics in the analyses and monitoring of biological samples. Microfluidic systems and electronics are complementary elements to develop a complete lab on a chip device. Fluidic samples need to undergo several elementary fluidic steps such as capturing, transporting, separating or mixing before been positioned on a sensitive region and be analysed. Electronic components are fundamental to pilot, detect, analyse and transmit the information to the outside. Recent articles combine deformable fluidic and electronics. An example is the realization of deformable antennas. [52]presents in their article a stretchable antenna for RF emission. In later papers from the same group[53], the antenna is used to monitor deformation since the resonance frequency of the antenna is proportional to the deformation.

Another raising topic in the same framework is on pressure sensitive devices. Handling objects by robot for instance impel the feeling of the object. This can be translated by a pressure sensitive skin. This captor requires being conformable to the fingers shape and flexible as the fingers move. Several groups have published articles on this topic. Array of capacitors is built on multi layers technology of elastic materials (PDMS) comprising microchannels filled with liquid metal (Galinstan). The array provides a precise localization of the object and the capacitor effect (which is proportional to the strain applied) provides the pressure on the object [54][55]. The S.Lacour group (EPFL) works on interfacing electronic components with the human body. For example she works on artificial electronic skin fabricated with soft materials and designed to detect simultaneously several macroscopic stimuli such as mechanical pressure and strain [56].

Foldable and stretchable materials open the way to new applications in the medical field through artificial organs. Silicone based materials are highly porous to gazes but not to liquids. A microfluidic network in those materials enables O_2-CO_2 exchange through a thin membrane. The work of J. Potkay et al. [57] reports a device enabling gas exchanges between air and blood made in stretchable material (PDMS) that could mimic artificial lungs.

Challenges

A number of flexible technologies are currently under investigations. Concerning soft and bendable electronics, according to [58] in 2012 6% of printed electronics will be conformal or flexible (mainly due to the rise of OLED for smart phones) and in 2022 this percentage will rises to 32%. The current trend in patches contacting the human body is toward the combination of intelligent fluidic and electronic devices. These systems must be light weight, take the shape of the skin, on which they are put, and follow all complex movements of the skin, explaining the need for elasticity. Typical examples are implants, intelligent tatoo, or robotics. Touch sensitive skin was originally developed for applications in robotics. Robots could be provided with pressure sensing ("touch") that would allow them to grip objects securely without damaging them. In addition, this field of soft and stretchable devices is now expanding toward biomedical systems for diagnostics or wellness. In those areas, the trends are in:

- Materials: The device must have a supporting layer with mechanical properties that match those of natural skin to avoid any discomfort resulting from long term wearing (permeable to gas and sweat) and the device must stick enough to the skin to hold the device during everyday life. Biocompatibility is an additional important property.

- Densification of sensors: Increase the number of sensors on a define surface that must be as small as possible to be able to measure for example temperature, heart rate, arterial pressure etc. on the same device.
- Part of the technology developed is tactile sensors that can include pressure sensors or strain sensors. The main application is in robotic but applications for medical implant are increasing.
- Wireless health monitoring devices: The sensors on the patch should be able to transmit and receive data from a personal smart phone. The information is sent to the person or his medical doctor directly reducing the reaction time and enabling monitoring of patient records.
- Energy harvesting/consumption: Wireless communication is favoured because it is more comfortable for the person having the device and also for his entourage (friends, family or doctors). The sensors must then have the lower consumption as possible, have batteries, low current and voltage for safety. For discrete measure, RF receptors are more and more developed. Antennas are directly built on the patch. Lot of efforts is provided to build a battery on the patch itself. They offer the opportunity to bring energy to the sensor, the sensor get the data and is able to send back the information to the receptor. In this field, the trend is to increase the distance between the emitter and the receptor.
- Wellness and safety sensors: Sensors like electrocardiogram developed for the wellness of a person during sport for instance or tiredness captors for drivers. Another increasing market concerns pulse oximetry sensors. The trend is to reduce their size, have them as less invasive as possible and be used by any person.

Patches have multitude of applications in biological monitoring, diagnostics or wellness. The challenge is to associate both, electronic and fluidic components on a same device and embark it on a person. The patch itself should not be invasive and as comfortable as possible because the person will often have it for a long period of time going from few hours to several days depending on the application. The challenge is to conceive a patch conformable with the holding surface (skin) taking into account the mechanical and physiological properties of the skin (elasticity, gas permeability, epidermal cells evolution or sweat).

The applications envisioned for soft and stretchable patches are:

Smart patches comprising sensors able to collect and analyse the sample and depending on the result, the patch should be able to take an action. For example, for patient with diabetes, the patch detects a high concentration of sugar in the blood so it injects precise quantity of insulin. Lot of challenges is present in this patch, how to detect the sugar concentration in real time and how to inject precise quantities. Anyway, one way is to take advantages of the mechanical properties of stretchable materials. Liquids can be stored under pressure and then be delivered by opening a valve. The movement of the skin can also be used to bring energy to the patch. Specific engineered designs with non-symmetric cavities could move the fluid in a direction. Valves could also be designed to block the fluid at a specific location on the patch. In this new area of stretchable microfluidic, a lot of functional fluidic components need to be developed (pumps or valves). The challenge is to take advantages of the mechanical deformability of the material to create self-energized components by taking advantages of the natural movement of the person. This approach will also reduce the total energy consumption of the patch. In addition, the patch can be used for drug delivery. Functionalized nanoparticles used for healthcare applications (like lipidots for cancer treatment) could be released into the human body through a porous membrane.

In order to transmit the information the intelligent and autonomous patch must communicate with an external interface like a smart phone. The communication should be wireless to add 1) comfort since there is no wire between the patch and the receiving device and 2) be more convenient, the information can be transmitted to a smart phone in any environment like for instance outside during a jog, analysed on the smart device and read by the user.

Intelligent patches can be envisioned as heterogeneous devices. An intelligent component that needs low consumption, liability and robustness and the sensor part with usually a large collecting area (to collect samples), transporting, separating, mixing and detecting functions.

Ultrathin silicon technology could bring the elements require for the intelligent part. It enables nanometric definitions and high performance, have a high density of elements while being flexible and stretchable. Ultrathin silicon can be transferred on polymer materials.

The sensor part does not need very high definition in the fabrication of its elements. It is envisioned in polymer to keep the flexibility and stretchability properties of the patch while being low cost. One of the challenges is the interconnections between the elements of heterogeneous devices. Electrical, fluidic or thermal elements on a given patch need to be connected. Since the medium is stretchable, conventional methods are not applicable and new approaches have to be engineered. In the spirit of industrialization, new industry procedures are required to manufacture high product volumes based on heterogeneous and flexible patches.

Conclusion

The future patch must be light weight, take the shape of the object on which it is fixed, and follow all complex movements of the host, taking advantage of those movements to harvest energy to the device, explaining the need for elasticity. Typical patch will have several functionality to collect, transport, analyse sample, deliver drugs and communicate with the outside (smart phone). The challenge is to package a patch (made of elastic materials) combining electronic (the intelligent components) and fluidic components (collecting, analysing samples and delivering drugs).

3.7 Micropumps and Actuators

State of the art

As far as actuators for healthcare are concerned, in the last years, most efforts concentrated on the development of micropumps for drug delivery. A very important number of realizations have been proposed, and main differences rely on the pumping mechanism and on the material in contact with the pumped fluid. The developments focused mainly on the fluidic characteristics of the micropumps such as the flow rate and the maximum sustained backpressure. Depending on the actuation principle, flow rates of some nanolitres per minute to some milliliters per minutes were achieved, and backpressures up to some 10kPa.

Mechanical micropumps based on piezoelectric actuation are the most popular and led to very nice results for example by the IMTEK [59]or by the Fraunhofer Institut [60]. Interestingly, piezoelectric actuation gave birth to the only industrial developments by Debiotech [61] and Bartels Mikrotechnik[62]. Nevertheless, other actuation principle are commonly used, such as the electromechanical [63], electrothermal [64], electrostatic [65], thermopneumatic [66] or electroosmotic [67] actuations among others.

Two material families are mostly employed for the fabrication of micropumps, silicon and polymers. Silicon is well known for its biocompatibility, the great precision of the fabrication processes (e.g. etching) leads to very high pumping accuracy, and the collective manufacturing is compatible with industrialization, although at high costs. Last but not least, it is possible to integrate sensors through the fabrication process [68]. On the other hand, polymers such as polypropylene or PDMS are more cost-effective. Moreover, biocompatibility is no longer an issue today. However, the still limited precision of the fabrication can be an issue for some applications where extreme pumping accuracy is required.

Some other examples of microactuators for health is an artificial sphincter (once again based on a micropump)[69], implantable hearing aids, [70] or surgical tools [71]. But curiously, other actuators for healthcare and wellness are barely found in literature, apart from microelectrodes for neurostimulation but that are treated in another chapter. This is quite surprising and should raise some questions.

Trends

Micropumps developments remain an attractive subject and more than 200 scientific articles were published in 2012. Miniaturization and the lowering of power consumption are clear objectives. Nowadays, drug delivery micropumps begin to integrate physical sensors that enable fluid and pump state monitoring [72] and thus a closed-loop control. It should allow for a better control of the delivery and thus an increased safety of the patient and in some cases a possible better therapeutic effect (e.g. convection enhanced delivery).

Miniaturization is of prime importance for the treatment of chronic diseases such as insulin delivery for diabetes, as patients need an increased comfort in their everyday life. Connected devices are emerging and show very promising perspective for a real-time personalized feedback on health.

- Soft devices with integrated electronics
- Autofocus eyelenses

Future

In the next years, personalized medicine is going to take always more importance. Drug delivery micropumps should follow this trend. One way is to integrate not only physical sensors but also physiological (ECG, blood pressure) and biological sensors able to control the therapeutic effect [73]. These sensors could be integrated directly into the micropump, or could be part of the global delivery system. In this aspect, future developments should consider the whole system not only the microcomponent, that is to say the electronics, the power source, the packaging. In this way of "thinking global", regulatory aspects such as biocompatibility, toxicity, clinical trials or CE marking should be taken into account from the beginning, as security aspects should (e.g. normally closed valves). Not negligible is also the securitization of the transferred data. In the same way, the global cost reduction in health should be taken into account in the development of new devices: manufacturing processes, material and reagents costs should be considered very carefully.

Actuators will benefit of the development of soft devices, and could be integrated into patches. For example, vibration of piezoelectric materials could be exploited for micromassages. Localized heating is also a possible interesting application. In this way, research teams will have to be able to work with various types of materials such as plastics, silicon, or paper based materials. Electronics could be based on organic electronics.

Negative would pressure therapy is a recently introduced treatment. Based on the application of a negative pressure onto the wound, it still relies on “classical” micropumps. The generation of this negative pressure should be miniaturized through the use of micropumps or of actuators based for example on chemical reactions.

In the field of glasses or eye-lenses, improvements should benefit of the recent development of auto-adaptive lenses for optics [74].

3.8 References

[1] Chen, Y.; Op de Beeck, M.; Vanderheyden, L.; Mihajlovic, V.; Grundlehner, B. and Van Hoof, C., “Comb-shaped polymer-based dry electrodes for EEG/ECG measurements with high user comfort “, 35th Intern. Conf. of IEEE Engin. in Medicine and Biology Society – EMBC, Osaka, Japan, July 2013

[2] Chen, Y.; Op de Beeck, M.; Vanderheyden, L. and Van Hoof, C. , “ Comparison of various polymer-based dry electrodes for high quality EEG/ECG measurements”, EMPC Conf. March 2013, Amsterdam, The Netherlands

[3] A 160μA Biopotential Acquisition ASIC with Fully Integrated IA and Motion-Artifact Suppression Nick Van Helleputte, Sunyoung Kim, Hyejung Kim, Jong Pal Kim, Chris Van Hoof, Refet Firat Yazicioglu

[4] Benabid, A.L., Pollak, P., Gervason, C., Hoffman, D., Gao, D.M., Hommel, M., Perret, J.E., De Rougemont, J., Long-term suppression of tremor by chronic stimulation of the ventral intermediate thalamic nucleus(1991) Lancet, 337 (8738), pp. 403-406

[5] Novel flexible Parylene neural probe with 3D sheath structure for enhancing tissue integration,Jonathan T.W. Kuo,a Brian J. Kim,a Seth A. Hara,a Curtis D. Lee,a Christian,A. Gutierrez,c Tuan Q. Hoanga and Ellis Meng, University of Southern California, Lab On Chip 13

[6] Implantable biomedical microsystems for neural prostheses, T. Stieglitz,M. Schuettler, K.P. Koch, IEEE ENGINEERING IN MEDICINE AND BIOLOGY MAGAZINE 2005

[7] Damien C. Rodger, Andy J. Fonget al., Flexible Parylene-based Multielectrode Array Technology for High-density Neural Stimulation and Recording. Sensors and Actuators B: Chemical, Vol. 132, Issue 2, 2008, pp. 449-460

[8] SU-8 based microprobes for simultaneous neural depth recording and drug delivery in the brain ,Ane Altuna,3*a Elisa Bellistri,3b Elena Cid,b Paloma Aivar,b Beatriz Gal,Javier Berganzo,a Gemma Gabriel,de Anton Guimera`,de Rosa Villa,de Luis,J. Ferna´ndez{ef and Liset Menendez de la Prida, Lab on Chip 2013

[9] A POLYNORBORNENE-BASED MICROELECTRODE ARRAY FOR NEURALINTERFACING, Allison E. Hess, Jeremy L. Dunning, Dustin J. Tyler and Christian A. Zorman, , Case Western Reserve University, International Conference on Solid-State Sensors, Actuators and Microsystems, 2007

[10] Imtek: Stieglitz et al. 2011

[11] Development of Microelectrode Arrays for Artificial Retinal Implants Using Liquid Crystal PolymersSeung Woo Lee, Jong-Mo Seo, Seungmin Ha,Eui Tae Kim, Hum Chung,and Sung June Kim Seoul National University, Investigative Ophthalmology & Visual Science, December 2009

[12] Imtek, Aachen University

[13] S. Musa et al., *Bottom-Up SiO2 Embedded Carbon Nanotube Electrodes with Superior Performance for Integration in Implantable Neural Microsystems*, ACS Nano, 2012, 6 (6), pp 4615–4628,

[14] Sauter-Starace, F. , Bibari, O. Berger, F., Caillat, P., Benabid, A.L.ECoG recordings of a non-human primate using carbon nanotubes electrodes on a flexible polyimide implant, CEA Leti , 2009 4th International IEEE/EMBS Conference on Neural Engineering 2009

[15] In vivo recordings of brain activity using organic transistors,Dion Khodagholy, Thomas Doublet, Pascale Quilichini, Moshe Gurfinkel, Pierre Leleux,Antoine Ghestem, Esma Ismailova, Thierry Herve, Se´bastien Sanaur, Christophe Bernard & George G. Malliaras, Ecole Nationale Supe´rieure des Mines, Nature communications 2013

[16] Maybeck, V., Edgington, R., Bongrain, A., Welch, J. O., Scorsone, E., Bergonzo, P., Jackman, R. B. and Offenhäusser, A. (2013), Boron-Doped Nanocrystalline Diamond Microelectrode Arrays Monitor Cardiac Action Potentials. Advanced Healthcare Materials
[17] Fabrication of Flexible Neural Probes With Built-In Microfluidic Channels by Thermal Bonding of Parylene, Dominik Ziegler, Takafumi Suzuki, and Shoji Takeuchi, JOURNAL OF MICROELECTROMECHANICAL SYSTEMS, 2006
[18] Implantable Biomedical Microsystems for Neural Prostheses,by T. Stieglitz,M. Schuettler, K.P. Koch, IEEE ENGINEERING IN MEDICINE AND BIOLOGY MAGAZINE 2005
[19] Interconnection of Multichannel Polyimide Electrodes Using Anisotropic Conductive Films(ACFs) for Biomedical ApplicationsDong-Hyun Baek, Ji Soo Park, Eun-Joong Lee, SuJung Shin, Jin-Hee Moon, James Jungho Pak,and Sang-Hoon Lee, Korea University, IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING 2011
[20] Omnetic Connectors Corporation, www.omnetics.com
[21] An implantable integrated low-power amplifier-microelectrode array for Brain-Machine Interfaces,Patrick, E., Sankar, V., Rowe, W., Sanchez, J.C., Nishida, T. , University of Florida, Annual International Conference of the IEEE Engineering in Medicine and Biology Society 2010
[22] Altuna, A., Bellistri, E et al., SU-8 based microprobes for simultaneous neural depth recording and drug delivery in the brain. Lab Chip, 13(7), 1422–1430., 2013
[23] SP Lacour, S Benmerah, E Tarte, J FitzGerald, J Serra, S McMahon, J Fawcett, Flexible and stretchable micro-electrodes for in vitro and in vivo neural interfaces, .Medical & biological engineering & computing 48 (10), 2010, pp. 945-954.
[24] In vivo recordings of brain activity using organic transistors,Dion Khodagholy, Thomas Doublet, Pascale Quilichini, Moshe Gurfinkel, Pierre Leleux,Antoine Ghestem, Esma Ismailova, Thierry Herve, Se´bastien Sanaur, Christophe Bernard & George G. Malliaras, Ecole Nationale Supe´rieure des Mines, Nature communications 2013
[25] van Beek, J.T.M. ; Verheijden, G.J.A. ; Koops, G.E.J. ; Phan, K.L. ; van der Avoort, C. ; van Wingerden, J. ; Badaroglu, D.E. ; Bontemps, J.J.M., Scalable 1.1 GHz fundamental mode piezo-resistive silicon MEMS resonator., IEEE International Electron Devices Meeting (IEDM 2007), pp. 411 – 414, 2007
[26] Grogg, D. ; Ionescu, A.M., The Vibrating Body Transistor, , IEEE Transactions on Electron Devices (IEEE TED), Volume: 58 , Issue: 7, pp. 2113 – 2121, 2011.
[27] Morris, D., Coyle, S., Wu, Y., Lau, K.T., Wallace, G., Diamond, D.Bio-sensing textile based , with integrated optical detection system for sweat monitoring, (2009) Sensors and Actuators, B: Chemical, 139 (1), pp. 231-236
[28] Schazmann , B., Morris, D., Slater, C., Beirne, S., Fay, C., Reuveny, R., Moyna, N., Diamond, D., A wearable electrochemical sensor for the real-time measurement of sweat sodium concentration, (2010) Analytical Methods, 2 (4), pp. 342-348
[29] Marchand, G., Bourgerette, A., Antonakios, M., Colletta, Y., David, N., Vinet, F., Gallis, C., Development of a hydration sensor integrated on fabric, (2010) Proceedings of the 6th International Workshop on Wearable, Micro, and Nano Technologies for Personalized Health: "Facing Future Healthcare Needs", pHealth 2009, art. no. 5754836, pp. 37-40
[30] Bandodkar, A.J., Hung, V.W., Jia, W., Valdés-Ramírez, G., Windmiller, J.R., Martinez, A.G., Ramírez, J., Chan, G., Kerman, K., Wang, J., Tattoo-based potentiometric ion-selective sensors for epidermal pH monitoring., (2013) The Analyst, 138 (1), pp. 123-128
[31] http://ec.europa.eu/environment/air/quality/standards.htm
[32] http://www.epa.gov/air/criteria.html
[33] http://www.epa.gov/ttn/atw/188polls.html
[34] A. Hierlemann, ISBN 3-540-23782-8 Springer Berlin Heidelberg New York.
[35] E. Comini, G. Faglia , G. Sberveglieri (Eds.), ISBN 978-0-387-09664-3, 2009, Springer.
[36] I.J.M. Erkens, M.A. Blauw, M.A. Verheijen, F. Roozeboom and W.M.M. Kessels, 'Room Temperature Sensing of O2 and CO by ALD Prepared ZnO Films coated with Pt Nanoparticles', ECS Transactions, 58 (10) 203-214 (2013)
[37] J. Laconte, C. Dupont, D. Flandre, J.-P. Raskin, IEEE Sensors Journal, vol. 4, 2004, pp. 670-680.
[38] J. Lee, W.P. King, Sensors and Actuators A: Physical, vol. 136, 2007, pp. 291-298.

[39] P.K. Guha et al., Sensors and Actuators B: Chemical, vol. 127, 2007, pp. 260–266.
[40] A.P. Lee, B.J. Reedy, Sensors and Actuators B: Chemical, vol. 60, 1999, pp. 35–42
[41] T. Iwaki, J.A. Covington, J.W. Gardner, IEEE Sensors Journal, vol. 9, 2009, pp. 314-328.
[42] E. Martinelli et al., Sensors and Actuators B: Chemical, vol. 161, 2012, pp. 534–541.
[43] E. Strelcov et al., Nanotechnology, vol. 19, 2008, p. 355502.
[44] J.D. Prades et al., Applied Physics Letters, vol. 93, 2008, p. 123110.
[45] W.C. Hinds, ISBN 978-0471194101, John Wiley & Sons, Inc.
[46] P. Kulkarni, P.A. Baron, K. Willeke (eds.), ISBN 978-0470387412, John Wiley & Sons, Inc.
[47] J. Phelps Black, PhD. dissertation , 2006, University of California, Berkeley (UCB/EECS-2006-193)
[48] J.D.Prades et al., Sens. and Act. B: Chemical, vol. 144, 2010, p. 1–5.
[49] V.V. Deshpande et al., Phys. Rev. Lett, vol. 102, 2009, p. 105501.
[50] http://www2.imec.be/be_en/press/imec-news/imecflexelect.html
[51] D.H. Kim et al. Epidermal electronics, Science 333, 838(2011)
[52] S.Cheng and Z.Wu, Microfluidic stretchable RF electronics, Lab on a Chip, vol 10, 23
[53] S.Cheng and Z.Wu, A microfluidic reversibly stretchable, large area wireless strain sensor, Advanced Functional Materials, vol 21, 12 pp 2282, 2011
[54] R.D.Ponce Wong, J.D.Posner and V.J.Santos,Flexible microfluidic normal force sensor skin for tactile feedback, Sensors and Actuators A:Physical, Vol. 179 62-69 2012
[55] J Dobrzynska and M Gijs, Polymer_based flexible capacitive sensor for three-axial force measurements, Journal of Mechanics and Microengineering, Vol. 23, 1,2013
[56] A Multifunctional Capacitive Sensor for Stretchable Electronic Skins D.P. Cotton, I. Graz, S.P. Lacour IEEE Sensors Journal, 2009, vol. 9, no. 12, p. 2008-2009
[57] Potkay JA, Magnetta M, Vinson A, Cmolik B. Bio-inspired, efficient, artificial lung employing air as the ventilating gas, Lab Chip. 2011 Sep 7;11(17):2901-9. doi: 10.1039/c1lc20020h. Epub 2011 Jul 14.IDTechEx report: http://www.ecnmag.com/blogs/2012/08flexible%20-barriers-1-billon-opportunity 2022
[58] IDTechEx report: www.ecnmag.com/blogs/2012/08flexible%20-barriers-1-billion-opportunity 2022
[59] Geipel A.;Goldschmidtoeing F.; Doll A. ; Jantscheff P.; Esser N.; Massing U.; Woias P.; “An implantable active microport based on a self-priming high-performance two-stage micropump”; SENSORS AND ACTUATORS A-PHYSICAL Volume: 145 Pages: 414-422 JUL-AUG 2008
[60] http://www.mikroelektronik.fraunhofer.de/en/press-media/microelectronics-news/article/high-pressure-micropump-for-demanding-applications.html
[61] http://www.debiotech.com/
[62] http://www.micro-components.com/index.php/home
[63] Trenkle F.; Haeberle R.; Zengerle R.; “Normally-closed peristaltic micropump with re-usable actuator and disposable fluidic chip”, Proceedings of the Eurosensors XXIII conference, 2009.
[64] Maloney J.M., Uhland S.A., Polito B.F., Sheppard N.F. Pelta C.M., Santini J.T., “Electrothermally activated microchips for implantable drug delivery and biosensing”, Journal of Controlled Release 109 (2005) 244– 255
[65] M.M. Teymoori, E. Abbaspour-Sani, Design and simulation of a novel electrostatic peristaltic micromachined pump for drug delivery applications, Sens. Actuators, A, 117 (2005) 222–229.
[66] S.-M. Ha, W. Cho, Y. Ahn, Disposable thermo-pneumatic micropump for bio lab-on-a-chip application, Microelectron. Eng. 86 (2009) 1337–1339.
[67] Y.-C. Su, L. Lin, Microelectromechanical Syst. 13, 75–82 (2004)
[68] WO201046728A1, “Mems fluid pump with integrated pressure sensor for dysfunction detection”, Debiotech S.A.
[69] Alexander F. Doll A.F., Wischke M., Geipel A, Goldschmidtboeing F., Ruthmannb O., Hopt U.T., Schrag H.-J., Woias P., “A novel artificial sphincter prosthesis driven by a four-membrane silicon micropump”, Sensors and Actuators A 139 (2007) 203–209
[70] Creutzburg T. and Gatzen H. H., “Simulations of an Electromagnetic Microsystem Used in Biomedical Applications” PIERS ONLINE, VOL. 6, N°. 4, 2010 375
[71] Watanabe Y., Maeda M., Yaji N., Nakamura R., Iseki H., Yamato M., Okano T., Hori S. and Konishi S., “Small, soft, and safe microactuator For retinal pigment epithelium transplantation”, MEMS 2007, Kobe, Japan, 21-25 January 2007

[72] Fuchs O., Fouillet Y., Maubert S., Cochet M., Chabrol C., David N., Médal X., Campagnolo R., "A novel volumetric silicon micropump with integrated sensors", Microelectronic Engineering 97 (2012) 375–378
[73] Meng E., Hoang T., "MEMS-enabled implantable drug infusion pumps for laboratory animal research preclinical, and clinical applications", Advanced Drug Delivery Reviews 64 (2012) 1628–1638
[74] http://www.minatec.org/en/vie-de-campus/minanews/breve/wavelens-cuts-cost-smartphone-autofocus?date_filter%5Bvalue%5D%5Byear%5D=2012

Chapter 4 Sensor Electronics & Signal Processing

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4.1 Introduction

Connected personal healthcare, or Telehealth, requires smart and miniature wearable devices that can collect physiological and environmental parameters during the daily routine of a user, which later can be used to extract biomarkers and to analyze personal trends for wellness, disease management, and independent living applications. Sharing information – both with medical professionals and within a community – requires on one-hand devices with wireless communication capabilities and on the other hand implementation of signal processing capabilities to minimize the data rate through wireless communication. On the other hand, development costs for medical devices are increasing dominated by the certification and qualification costs. Hence, integrated solutions that can address multiple applications will enable cost reduction in wearable devices and enable the wide acceptance range among the community. System-on-chip technology can enable the development of miniature size and highly integrated devices. However, low-power dissipation with medical grade data quality is an on-going challenge.

Today's sensor and transducer electronics are driven by three main trends: cost reduction, lowest power consumption and increasing sensing accuracy. Continuous cost reduction is the main driver for enabling mass market and semiconductor industry has an excellent track record in cost reduction. The ITRS roadmap predicts continuous cost reductions in the next decade especially for highly integrated products which integrate analog, RF, power, digital, memory, and also sensor electronics on chip ('More than Moore'). This is the key economic requirement to enable broad adoption of electronics not only at the hospital and doctors office, but also for preventive and monitoring health care at the patient and in daily live.

Besides the economic requirements, the acceptance by the user is also defined by comfort and ease-of-use. The smaller the device, the more obtrusive it is. However, the battery rather than the circuit components vastly defines the size and weight of the devices. This requires the development of ultra-low-power integrated systems that requires minimal energy for a given task so that the system size and weight can be miniaturized. Finally, the need for increasing signal accuracy makes it challenging to meet cost and size requirements of smart and miniature wearable devices.

This chapter focuses on one of the key – and historically one of the most power consuming – building blocks of smart systems – Sensor & Transducer Electronics and the signal processing. Emerging strategies to achieve low-noise and low-power dissipation will be reviewed and trends will be discussed. Finally, application highlights and emerging IC technology will be presented.

4.2 Signal characteristics

Healthcare and wellness applications require variety of signals including bio-signals, bio-markers, environment variables, etc… Bio-sensors and chemical sensors (gas sensor) can be used in everyday life (monitoring of CO levels at home, alcohol controls for engine drivers), in the workplace (checking of toxic gases), and in healthcare applications (monitoring of gases in hospitals, breath testing to detect volatile organic compounds whose combination represents a disease signature [1]. These sensors rely on different methods, depending on the mode of the signal transduction: physical transduction (magnetic, calorimetric, piezoelectric, piezoresistive) or chemical transduction (optical, electrochemical, electro-optical).

In spite of vast amount of different sensors, all the processed signals are related to physiological signals (neural, muscular, cardiac), biologic parameters (ions, enzymes concentration) or environmental parameters (temperature, pressure, gas concentration), so they are generally low frequency, and low amplitude signals.

For instance, movement analysis use accelerometer sensors and many studies tried to find the minimum signal characteristics to discriminate the different postures of lying, sitting and standing. Veltink et al[2] demonstrated that the bandwidth of the movement data is less than 3Hz, for a +/-2g range. Higher frequency signals are actually movement's artifact signals, which need to be removed. For such a range, Lyons et al[3] reached more than 90% accuracy with a 12bits resolution. More recent studies have even proved that a 20Hz sampling frequency and 12 bits resolution were enough for analyzing human movements[4][5].

Similarly, physiological signals have a rather low-frequency content as well (Figure 4.1) On the other hand, rather small amplitudes of these signals make them very challenges to monitor, especially ambulatory conditions, requiring rather power hungry precision interface circuits.

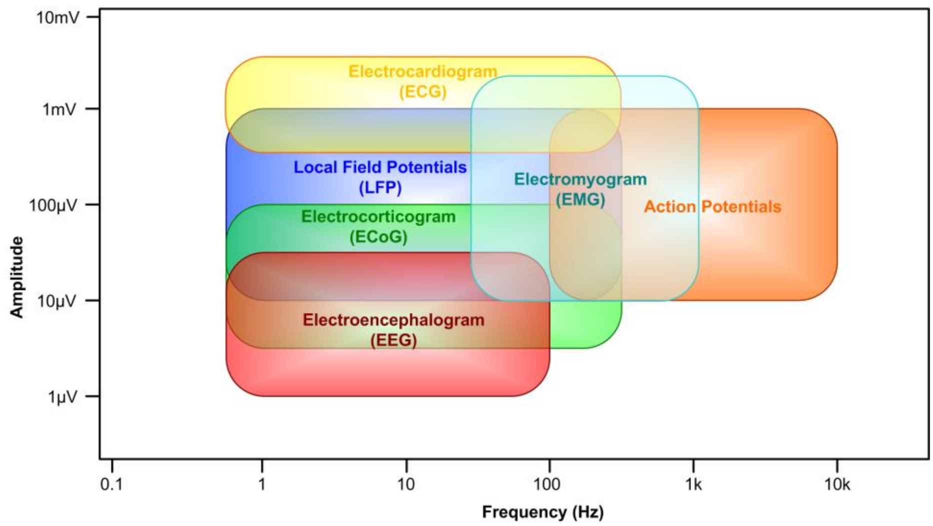

Figure 4.1 Amplitude and Frequency characteristics of different biopotential signals

As for the environmental sensing and gas sensor, despite concentrations variations vary very slowly, the sensor readout bandwidth can be very high, depending on the transduction principle. The targeted concentrations depend on the gas type. According to Fanget et al.[6], they vary from 1ppb to 20ppm for formaldehyde (molar mass 30.02g/mol) and from 500ppm to 40000ppm for CO_2 (molar mass 44.01g/mol).

4.3 Sensor front-end architecture

The purpose of the sensor front-end is to interface with the biomedical and environmental sensors and extract signal with the required accuracy. In general, a sensor interface consists of 3 blocks: low-noise instrumentation stage, anti-aliasing filtering stage, and analog-to-digital conversion stage.

4.3.1 Low noise instrumentation

Low-noise instrumentation is use to acquire signals from a transducer. In physiological signal acquisition, transducers can be as simple as an electrode converting ionic current into electronic current, or more complex as in a transducer such as acceleration to capacitance, gas concentration to frequency, etc.

The main specifications for an Instrumentation Amplifier (IA) are its accuracy (or noise), and power dissipation. For a low power budget, especially in ambulatory applications, this stage has to make a trade-off between noise constraints (resolution) and power consumption. In literature, a Noise-efficiency-Factor (NEF) is used to summarize this trade-off:

$$NEF = v_{ni}\sqrt{\frac{2 \cdot I_{tot}}{\Pi \cdot \mathrm{U}_t \cdot 4kT \cdot BW}}$$

v_{ni} is the total input-referred noise over a bandwidth, BW. I_{tot} is the total power consumption, U_t is the thermal voltage, k is the Boltzmann's constant and T is the temperature.

Various instrumentation amplifier architectures exist in the state of the art. We will review those architectures and mention their advantages and disadvantages. Finally, directions in emerging Ias are presented.

An industry standard instrumentation amplifier is called "3-opamp Instrumentation Amplifier", (Figure 4.2) Opamps A1 and A2 buffer the differential input and provide high input impedance. The first stage of the architecture has a common mode gain of 1, and differential gain of (1+R1/RG). The second stage is used to reject the common mode signals from the first stage and presents a differential gain of unity. One of the main benefits of the architecture is its very high input impedance. However, it has a high power consumption as it uses three opamps driving a resistor feedback network and has a limited CMRR performance (<70dB) defined by the mismatch of the resistors at the second stage, R_2*.

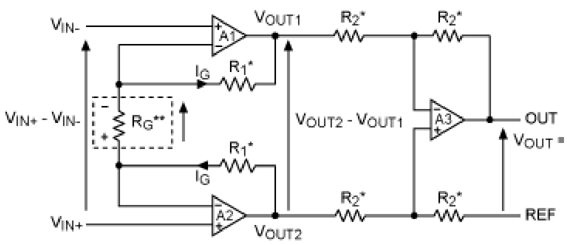

Figure 4.2 Industry Standards 3-opamp Instrumentation Amplifier

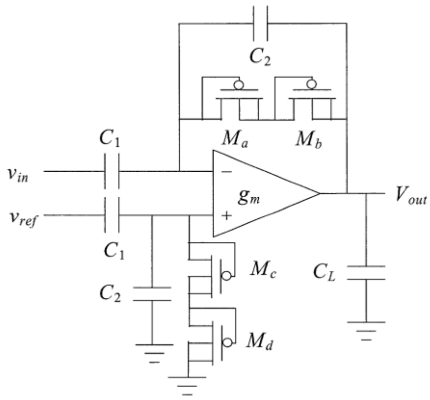

Figure 4.3: Capacitive Feedback Architecture

Due to the performance and power dissipation limitations of this architecture, different instrumentation amplifier structures have been emerging during the last 5 years. (Figure 4.3) shows a rather popular architecture called a capacitive feedback IA architecture [39]. Since, this architecture has only one opamp with a capacitive feedback network. Hence, it consumes much lower power than the standards 3-opamp one. However, this architecture, also, has a limited CMRR performance (<70dB) due to limited matching between capacitors.

In order to improve the performance, chopper modulation technique has been widely applied to precision instrumentation. However, application of this technique to biomedical signals is not possible due to the large polarization voltage of the bio-potential electrodes requiring rather a large dynamic range. Hence, chopper stabilized amplifiers, with DC servo feedback have emerged during the recent years, which enable the use of chopper modulation for biomedical signal acquisition. Figure 4.4 shows the architecture of such an amplifier [44]. The main advantage of this architecture is that it has an extremely high CMRR (>120dB) and the flicker noise of transistors can be filtered from the measurements.

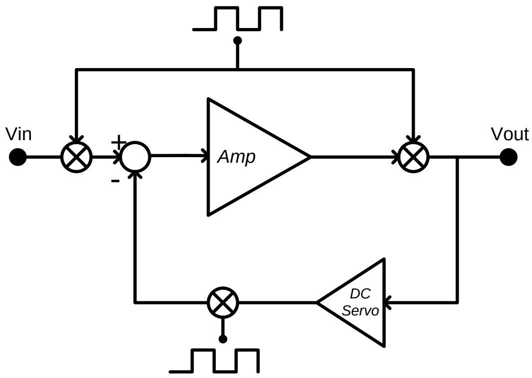

Figure 4.4 AC-coupled chopper stabilized Current-Feedback Architecture

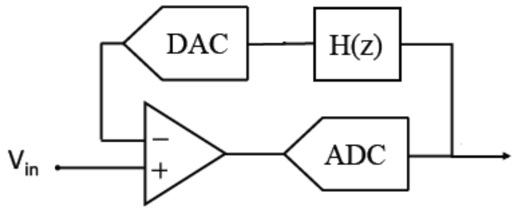

Figure 4.5: Integrated IA-ADC Architecture at 0.5V supply

In the recent years, with the increase in demand for portable devices, there is a need for ultra-low voltage supply (<0.7V), integrated IA-ADC low area architectures. In the previous examples, obtaining large on-chip time-constants by passives facilitates extremely low power consumption but also consumes large area. Integrated IA-ADC architecture, as shown in Figure 4.5, implements the needed time-constant in the digital domain, thus reducing area [45]. Here, apart from the first amplifier block, rests of the blocks are mainly digital in nature. This not only facilitates functioning at 0.5V supply and low power consumption but also eases the technology portability of the design. However, the input-referred noise figure and the CMRR performance decrease while functioning at such low supply voltages. Co-design of the IA and ADC makes such architectures relatively more complex to design and also, they cannot be used as plug-and-play for different bio signal readouts.

In many bio signal applications, multi-channel monitoring was proved necessary to achieve better physiology comprehension and event detection. The major drawbacks in these multi-channel chips are the increase in area and power consumption, and the risk of crosstalk between channels. To reduce the cross-coupling problem, one solution is to minimize wire parasitic by integrating the first stage amplifier on the sensor, this significantly reduces the effect of parasitic crosstalk. Such approach is being used both for scalp EEG measurements (see section 4.7.2), where part of the readout is placed on the sensor for pre-amplification, and also for high density neural arrays (see section 4.7.1), where the pre-amplification is happening right under the recording site.

4.3.2 Analog-to-digital conversion

To optimize power and area budget, multiplexed architectures are used to mutualize processing resource. Since bio-signal are low bandwidth, the analog-to-digital converter can be shared between different channels[9]. In the field of healthcare applications, the Successive-Approximation-Register ADC is a good candidate. For medium-frequency applications (few kHz), it actually presents a good compromise between power and resolution, and many studies tend to optimize its performances[10].

In actual works, pre-processing stage is most of the time monolithically integrated for a better density integration and energetic optimization. The corresponding chip is consequently a mixed-signal circuit, with analog blocks for amplification, anti-aliasing filtering and digital conversion, and logic for additional filtering and data processing. To cope with low noise and dynamic range specifications, the chips are most of the time implemented on rather old integrated technologies: from CMOS350nm down to CMOS 130nm (more rarely CMOS65nm). These technologies actually offer high power supply voltages which allows high voltage gain without signal saturation, and which releases constraints on analog-to-digital input noise. These advantages from an analog point of view are at the price of power performance and integration density. These technologies are actually not optimized for high density data processing and that is the reason why data processing is mainly done off-chip. More recently, with the emergence of wireless systems and especially implanted systems, the data flow had to be reduced to diminish the data transmission power budget, most of time predominant in the whole system power budget. The filtering was developed not only to diminish noise effects but also to extract signals details to realize on-chip classification. In this mixed-signal context, thin-film technologies can be an opportunity to meet analog high gain requirements as well as high integration density of digital blocks.

4.3.3 Co-integration

Besides the classical direct measurements approach, more and more works describe co-integrated architectures. This is driven by both form factor performance, and energy needs. Moreover many health care markets will be only affordable for the complete European population if good cost control of medical devices is simultaneously realized with a precision needed by the medical application. Co-integration approaches have a significant leverage to optimize all these parameters. First of all, a system on chip or system in package is in almost all cases the solution with the smallest form factor for the application. Second, the power for communication between chips is minimized when the capacitive load of the interface circuit is minimized. Third, the performance and resolution of sensor systems can be drastically increased when the read-out of different sensors are combined to a multi-sensor signal. Last but not least the cost, i.e. of system on chip products in most cases is lower than heterogeneous co-integration. Several technical approaches to optimize different aspects of the above mentioned parameters are discussed in the following.

First realizations reported switched-capacitor systems with the capacitive sensor inside the first amplification stage[11]. In these architectures, the M/NEMS parameters are part of the transfer function: low-pass or band-pass filtering. Co-design of the sensor and the readout architecture offers the best opportunity to meet challenging performances. To improve systems linearity and to take advantage of the high-Q performance of M/NEMS, the sensor can be embedded in closed-loop architecture. Using control theory principles and digital corrector, the readout architecture becomes more accurate, linear and adaptable to sensor variations and ageing[12]. Besides the advantages of closed-loop architecture, sensors driving circuits integration is still challenging. Because of the micro/nano sensor down scaling, the sensor output drive generally needs high voltage commands. These HV drives generate a low-level proportional-to-resistor signal on the sensor. For monolithic integration, the sensor interface should be designed on CMOS LV/HV process, at the expense of design complexity and power consumption.

Last evolution in healthcare sensors is the development of electrochemical sensors, where the potentiometric approach is preferred: a device is fabricated with a gate electrode which is sensitive to the detected substance. In ion-selected field-effect transistor (ISFET), drain-source current is proportional to pH, whereas is ENFET, drain-source current is proportional to an enzyme concentration. Main drawback of these sensors is that they are not compatible with CMOS processes.

4.4 Adaptive sensor readout circuits

Next generation of readout circuit will have to comply with an increasing number of sensor outputs. For example, NEMS based MicroElectrodes Arrays (MEAs) will embed more than one thousand electrodes. Increasing the number of readout circuits on a same die will put harsh constraints on both silicon area and power consumption of readout circuits. Some biomedical applications such as BCI, heart pacemaker or glucose meter use implanted devices for which the replacement of batteries is uneasy. The ultimate goal is the design of fully autonomous sensor systems that harvest their energy from their environment. A photovoltaic based biomedical sensor has already been published[13] as well as work on glucose fuel cell[14]. Obviously, these applications will require ultra-low power readout circuit ensure long lifetime.

As of today, readout circuits convert sensor output at a given rate and a given accuracy and have a fixed data throughput, independently of its environment that is to say the available energy and the information sparsity at sensor output. Great power savings are to be expected from systems fully aware of their environment and which can adapt their behavior subsequently.

4.4.1 Adaptation to power level

While Digital Voltage and Frequency Scaling (DVFS) is a well-established technique to lower digital circuit power consumption and adapt their performance to energy availability, there is no equivalent technique in analog domain. Nevertheless, it could be interesting to adapt the readout circuit precision to power level to ensure continuous service, providing high resolution when high power level is available while providing a degraded performance when low power level is available. This could be accomplished thanks to energy-event architectures which efficiency has already been demonstrated in the power management circuits dedicated to autonomous sensors[15][16].

4.4.2 Adaptation to interface quality

Because the first stage is connected to the sensor, it must be compliant with input impedances dispersion. In neural, cardiac and muscular applications, biomedical sensor output quality depends strongly on the quality of the interface between the sensor and the biological tissue. The production of glyal cells around MEAs degrades measurement of neuron activity in BCI applications.. Therefore, having a measure of signal quality, and generally speaking of measurement conditions (for example temperature), is highly desirable in order to fully appreciate sensor readout output. This can rely on extra sensors dedicated to the monitoring of measurement conditions. Some studies now relate on-chip impedance measurements, to optimize the dynamic range of the readout circuit, and follow the electrode-to-tissue contact in case of in-vivo applications[17].

4.4.3 Adaptive to Signal Activity

Readout circuit transmits digitized version of the sensor analog output to the DSP that will take in charge classification tasks. As of today, readout circuits digitize sensor output signal, even in the absence of any useful information. This is responsible of a huge waste of energy as the readout circuit transmits a flow of useless data.

Limiting the readout data throughput is highly desirable to save power. It is thus highly desirable to design event-driven readout architecture, transmitting information only when pertinent signal is present at sensor output.

A first direction could be found in the design of wake-up readout sensors able to detect pertinent information at sensor output and that will awake the principal readout sensor to measure and transmit the information. Under Hibernets project[18], a wake-up sensor has been designed which is sensitive to the spectral signature of the sensor output. It is worth mentioning that wake up readout solution is efficient only if their power consumption is kept very low compared to the readout consumption. Other examples for selective data digitization include the usage of thresholding based techniques and Teager energy operator (TEO) for neural spike acquisition [78][79].

A second direction consists in designing event-based ADC architectures which output rate depends on the signal activity at its input. First possible implementation lies in the so called asynchronous ADCs that output data only when their inputs cross defined comparison levels as shown in Figure 4.6

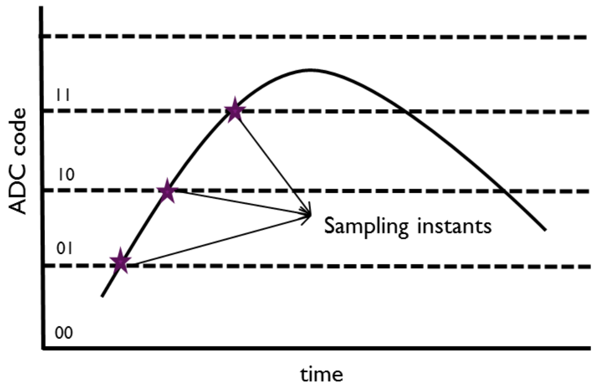

Figure 4.6: Level crossing based analog to digital conversion

Other solutions include adapting the sampling clock period of conventional ADCs to the information changing rate as shown in Figure 4.7 [20][21] and the specimen ECG signal sampled adaptively is shown in Figure 4.8. The information rate in the signal can be detected by using activity detection circuits, which include the simplest techniques like computation of derivative to detect the presence of high frequency content to more complicated techniques such as using short time Fourier transform. For the approach to be truly beneficial, the power consumption of the activity detection circuits should be much lower than the power savings obtained by adaptive sampling. A third direction consists of providing compression directly in the readout circuit to limit data throughput. This could be done by adapting the ADC resolution to the variation rate of the input signal. Several implementations are under investigation from which the use of logarithmic ADC seems promising[22].

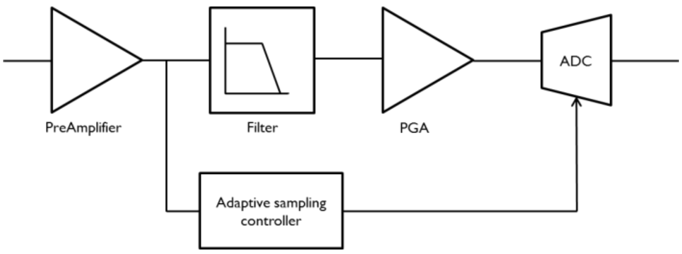

Figure 4.7: Analog front end with adaptive sampling

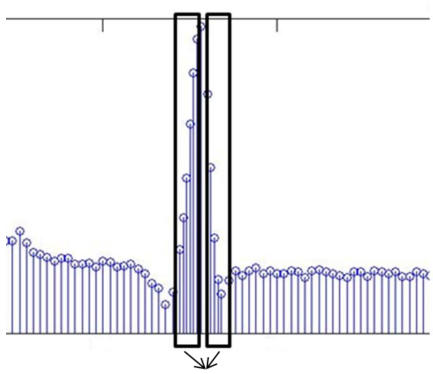

Figure 4.8: Adaptive sampled ECG segment

4.5 Integrated Control and Signal Processing

A sensor/actuator node requires embedded processing to handle control, signal processing as well as protocols. The systems targeted by this working group will be energy constrained with various operating duty cycles. In this context, processors with very high energy efficiency, targeting the Internet of Things, have already been introduced like the MSP430, the ARM M0+, or the CSEM icyflex2. For battery supplied circuits, extensive power gating, sleep and wake-up modes are required. Adaptive Voltage and Frequency Scaling (AVFS) targeting an optimal energy point is also a key technique whose interest has to be evaluated considering the application scenario. In addition the following emerging techniques are very promising for the targeted applications.

4.5.1 Near/Sub-threshold computing

It has been shown that it exists an optimum energy point for a computing system. This point depends on the technology as well as on the architecture and the activity[23]. Seeking for this point, several demonstrations of sub-threshold computing have been made, to the cost of a very low operating frequency. The current consensus is that near-threshold computing brings an optimum performance/energy trade-off. ST and MIT have for instance demonstrated a very efficient 16 and 32 bit microprocessor with an optimum energy point of 10.2pJ/cycle at 0.54V power supply; the same circuit, by setting a nominal power supply was also capable of a peak performance of 82.5 MHz at 41.7pJ/cycle[24]. At such low voltages, a key challenge is SRAM stability and retention. To overcome an unachievable compromise with the standard 6 transistors cells, it is frequently useful to move to an 8 transistors cells, like in the previous paper. Another example can be found in [25].For systems that will require performances adjustable according to the on-going application requirements or to the available energy, wide to ultra-wide tunable operating voltages are under consideration. However, working close to the threshold voltage amplifies the variations impact. To cope with, embedded dedicated sensors allowing a fine control are required[26][27]. In this global scope, advanced thin film technologies like FinFet or FDSOI, thanks to its better device electrostatic control could bring large tunability as well as hundreds of MHZ operating frequency at very low supply voltage. However those technologies have large NREs and thus require very large volume applications.

4.5.2 Co-processing and specialized co-processors

As specialized hardware brings large energy saving compared to regular processors, to the cost of flexibility, a compromise has always to be found. For applications involving quite a significant signal processing, embedding energy efficient DSP (Digital Signal Processor) in addition to the microcontroller leads to an interesting intermediate point, like in [28],[29]. A custom DSP, which consists of 4-way SIMD processor architecture and hardwired accelerate unit optimization on the characteristics of the target application, provides configurability and intensive computation [46]. Instead enhance the processor power, a special hardware accelerator for the advanced function such as FFT [47] and ICA [51] are integrated to perform the complex operation without burdening the main processor. Finally, embedding some reconfigurable logic to handle some part of the control or the calculations can also induce significant energy saving, one of the key challenges being in this case the link between hardware and software [46].

4.5.3 Adaptive and imprecise architectures

Another way to tune the performances to the on-going application requirements is to adapt and optimize the processing architecture. At a very high level the ARM big.LITTLE concept allows a transparent switching between two cores: a small energy efficient one with limited performances, and a large powerful one.

Today's ultra low power embedded MCU systems go a step further: peripherals are operating autonomously using DMA together with specialized digital peripherals while the main processor sleeps during sensor data acquisition. When the main processor is active it is supported by variable precision arithmetic units for low energy, high throughput number cruncing. This includes techniques like dynamic adjustment of the data-path width has been proposed, like in [32]. Going one step further, approximate or inexact circuit design techniques have been introduced for error-tolerant applications. In this case, a relaxed fidelity requirement provides performance and energy benefits[33][34]. Another efficient adaptativity is brought by the asynchronous or event-driven processors[35]. Finally, data-driven approaches such as neural-network and machine learning has also emerged. It provides the high accurate analysis tool than analytical methods and emerges the customization system by user-specific models [66][83].

4.6 Assisted Signal Processing and Compressed Sensing

Efficient task partitioning between the analog and digital domains is a vital consideration for the system power reduction given the fact that majority of the biopotential acquisitions systems are mixed signal in nature. It has been shown in [80] that for imprecise computations where signal to noise ratio is limited to 50-60 dB analog computation could result in lower power consumption. So, it is possible to reduce the system power consumption by carefully offloading the tasks that require limited SNR to analog domain and perform rest of the tasks in digital domain. An example for such system is demonstrated in [69] where the ECG signal is bandpass filtered in analog domain to detect the presence of QRS complexes before performing a more sophisticated and power consuming QRS complex search in digital domain. The optimum way of task partitioning is dependent on the application and needs to be evaluated on case by case basis.

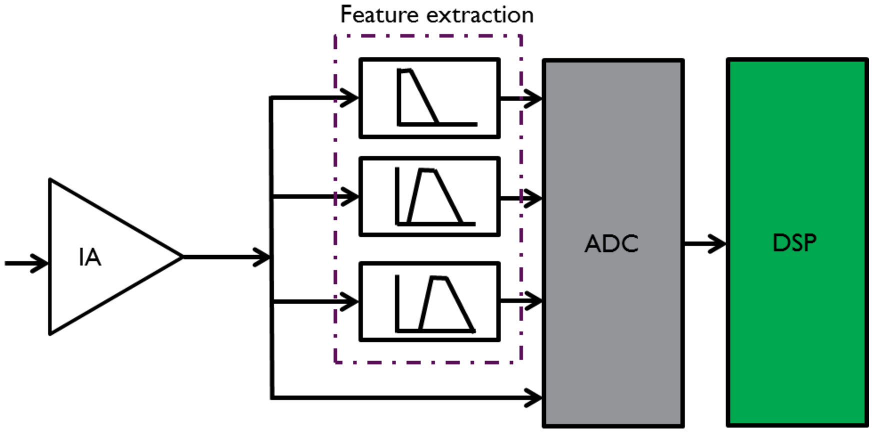

Figure 4.9: Mixed signal system with feature extraction in analog domain

The other application domain where the assisted signal processing is gaining attention is in feature extraction and classification. Feature extraction and classification forms an important aspect of biomedical systems, where in the signal is analyzed to distinguish between the normal and abnormal physiological conditions. Classification requires *feature vectors* which typically include the spectral characteristics of the signal. It has been shown in [81] that modest resolution of 8 bits is sufficient to achieve reasonable classification accuracy and therefore feature extraction could be implemented in analog domain at low power levels while the classifier could be implemented in digital domain as depicted in Figure 4.9.

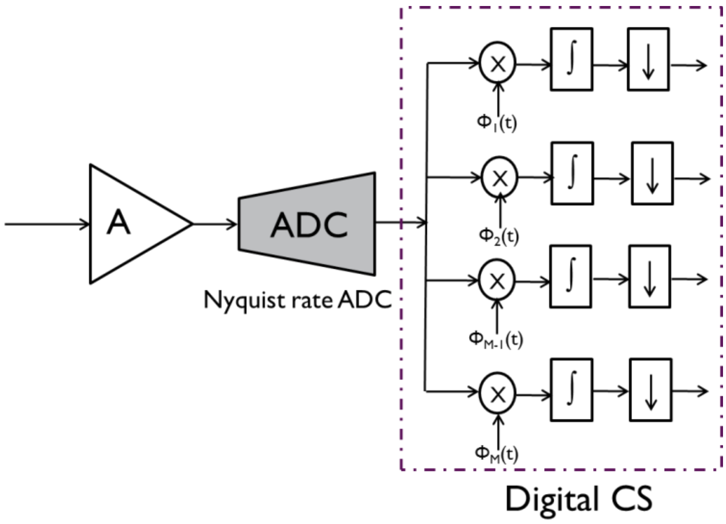

Figure 4.10: Digital compressed sensing implementation

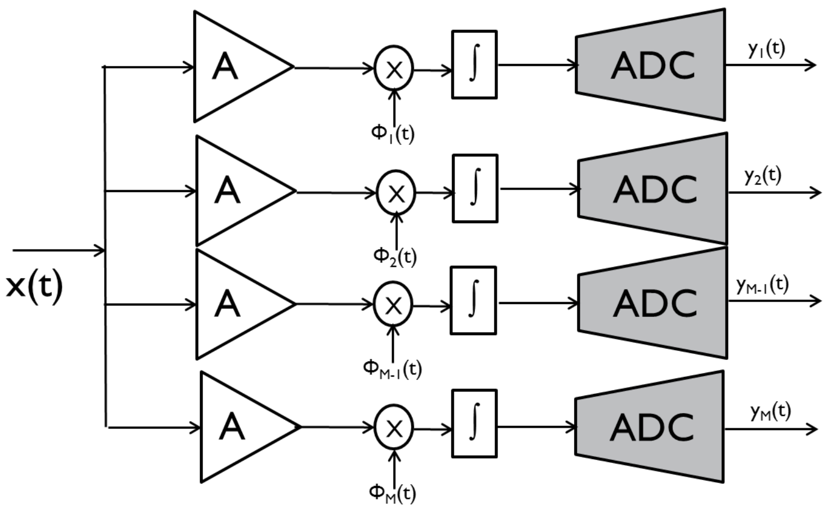

Figure 4.11: Analog compressed sensing implementation

Compressed sensing is a novel signal acquisition method which can be used to recover sparse signals by sampling at rates far below the conventional Nyquist rate. This can lead to significant power savings in the analog to digital conversion and transmission. Compressed sensing can be implemented either in digital domain as shown in Figure 4.10 or in analog domain as a parallel Random Modulation Pre-Integration blocks as shown in Figure 4.11. It has been demonstrated that compressed sensing is potentially attractive for real-time compression of electrophysiological signals like ECG or Neuron activity and that some signal processing can be very efficiently achieved in the compressed domain [36][37]. In this latter work, EPFL designed a new generation of ultra-low-power microcontroller embedding dedicated Compressed Sensing operations which led to a very significant node lifetime improvement. For the signals that are sparse on frequency domain (such as PPG), compressed sensing can be implemented as random sampling, which enables to duty-cycle the photodiodes with smaller duty ratios, thereby significantly reducing the power consumption as demonstrated in [82].

4.7 Emerging Integrated Systems

4.7.1 Implantable Systems

Brain Implants

Neural implants are medical devices that are brought in contact with a specific brain region to electrically stimulate and/or record signals from single neurons or groups of neurons. Neural implant applications can be classified in three categories: sensory prosthetics, brain pacemakers and brain computer interfaces (BCIs). The first category makes use of sensors (e.g. sound, image, tactile) and electrical stimulation in order to restore the ability to perceive a certain defective sensory modality. Brain pacemakers are medical devices for electrical stimulation applied to different brain areas, and are mainly used for the treatment and prevention of epilepsy, Parkinson's disease, major depression and other diseases. BCIs involve creating interfaces between neural systems and external devices, making use of neural stimulation and recording, artificial prostheses or other assistive apparatus; their main use is for the restoration of a lost or damaged motor function which is, in normal conditions, controlled by the brain.

The rapid progress of neuroscience research has created a need for neural interfaces capable of monitoring the activity of large numbers of neurons. Such devices are composed of a neural probe connected to an integrated circuit for recording neural signals from multiple electrodes and transmitting the recorded data to external equipment's. Emerging technologies are trying to address small form-factor requirements and low power-consumption constraints, while providing high spatial and temporal resolution. Furthermore, implantable neural interfaces are pursuing two main goals: (i) replacing hardwired connections with flexible cables or wireless links in order to reduce cable tethering and infection risks, and (ii) enabling local processing of neural signals in order to reduce noise coupling and improve signal integrity [38].

The interconnection of neural probes with application-specific integrated circuits (ASICs) to form fully implantable devices poses important power and area limitations to the circuit design and creates several tradeoffs among different circuit blocks and specifications. For instance, implantable systems may dissipate only very low power in order to avoid heating of the surrounding tissue [39], but low-power telemetry usually achieves only limited bandwidths, making the transmission of many recording channels difficult. In the last years, researchers have proposed different kinds of neural interface architectures to deal with such tradeoffs [40]-[50]. They are usually composed of low-noise neural amplifiers, filters, multiplexers, ADCs and wired/wireless telemetry circuits.

The current trend in neural interfaces is to achieve massive parallel recording (e.g. Figure 4.12 [50]) while minimizing power and area consumptions (e.g. Figure 4.13 [49]). This requires the development of low-power circuit techniques, efficient data management and smart power scheduling [38]. Wireless communication has received great attention due to its benefits in fully-implantable applications [41], [43] , [49]. However, this technology is still relying on data reduction techniques in order to be able to transmit the information of large number of channels, which is not useful for applications that require the full raw data.

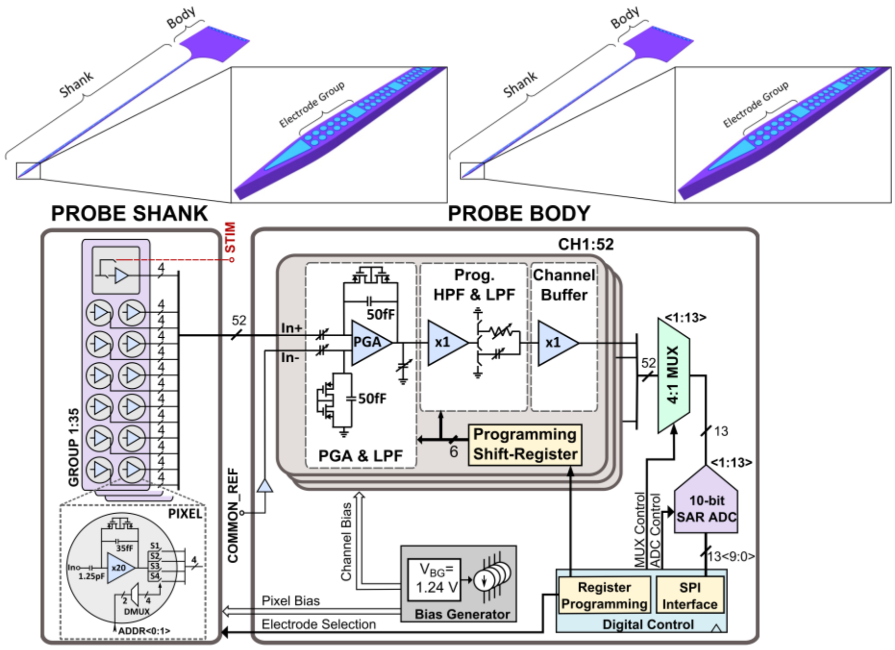

Figure 4.12: An implantable active-electrode CMOS neural probe [50] .

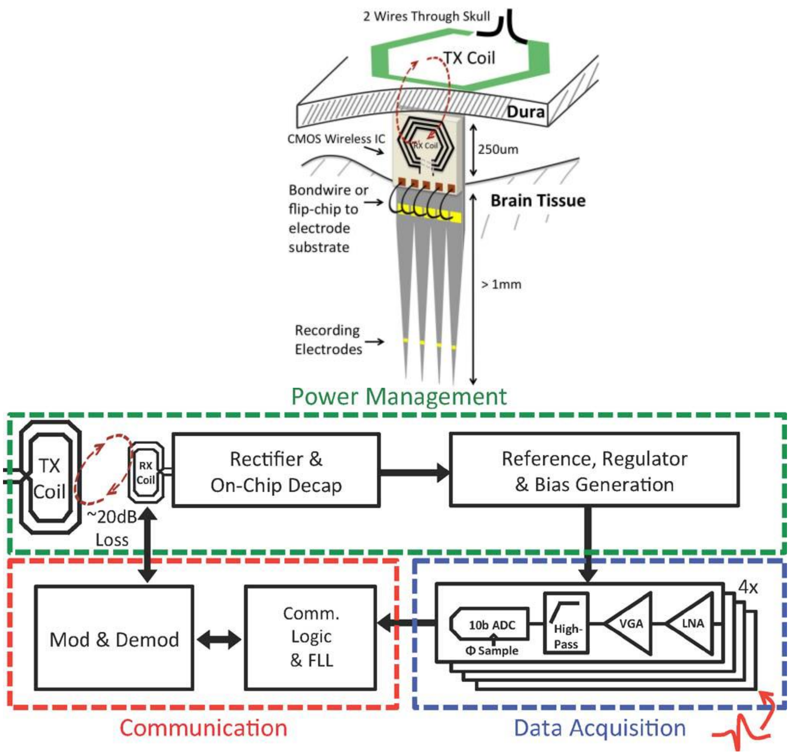

Figure 4.13: A fully-integrated, miniaturized wireless neural sensor [49].

4.7.2 Electronis for Wearable Systems

Integrated Circuits for EEG Monitoring

The emerging wearable EEG system for personalized healthcare and lifestyle applications must facilitate the high-quality EEG recording in a non-invasive and comfortable manner. Various EEG ICs have been developed towards ultra-low-power, extended battery lifetime, better signal integrity, extended functionality, and improved user comfort.

A classical AC-coupled capacitive feedback amplifier has been implemented for EEG application [52]. The use of capacitive feedback and MOSFET pseudo-resistor implements a sufficiently low high-pass corner (<0.5Hz), while the input coupling capacitor rejects any electrode offset from the subject. Several designs using the same architecture were reported to further improve the noise efficiency factor (NEF) and programmability [53][54]. [55] further improves the NEF of the front-end amplifier to 2.24 by connecting PMOS and NMOS input transistors in parallel. This amplifier also uses tunable pseudo-resistor to reduce its total harmonic distortion (THD). The whole 32-channel system, including programmable gain amplifier (PGA) and 12b SAR-ADC, consumes 22μW from 1V supply. In the future, the CMOS technology scaling (<90nm) of analog front-end IC enables a lower supply voltage (<1V) and extends the use of digitally-assisted analog ASICs.

For better signal integrity, various chopping techniques have been applied to this AC-coupled capacitive feedback architecture for less $1/f$ noise and better common-mode rejection ratio (CMRR). The chopper-stabilized EEG amplifier in [56] achieves 100nV/sqrt(Hz) input-referred noise and 105dB CMRR. This topology applies the chopper modulation before the input capacitor and implements a DC feedback path to compensate the electrode offset up to 50mV. [57] uses an alternative chopping technique in the EEG amplifier, where the chopper modulation is performed after the input capacitors, i.e. inside the feedback loop. This approach preserves the rail-to-rail electrode offset rejection capability, while still achieving a high input impedance at the cost of limited CMRR (60dB). [58] implements a current-balancing instrumentation amplifier (CBIA) with chopper modulation, which achieves 60nV/sqrt(Hz) input-referred noise, 1GΩ input impedance and 120dB CMRR, the DC-servo loop also compensates 50mV electrode offset.

One of the major problems in wearable EEG recording is the use of gel electrodes. This requires significant preparation time to facilitate EEG recording. Active-electrode based EEG recording systems are gaining popularity during recent years. Such systems enable the use of gel-free, or dry electrode for improved user comfort. Active electrodes (AE) are simply the co-integration of the preamplifier and the electrode. The low output impedance of the pre-amplifier effectively reduce the cable motion and mains interference. As a conventional active electrode solution, [59] uses a voltage buffer as an AE for high input impedance and CMRR. Besides, its analog output is combined with supply in a single wire. Recently, [60] and [61] implements AE with pre-amplifiers. The voltage gain of AE relaxes the noise requirement and thus reduces the power consumption from the back-end readout circuits. However, the gain mismatch between AEs limits their inter-CMRR. To compensate the CMRR of multiple AE pairs, common-mode feedback (CMFB) in [60] or common-mode feedforward (CMFF) in [62] was implemented (Figure 4.14, Figure 4.15). Both methods feed the common-mode signal back to the input of EEG amplifier, instead of the subject, to improve the stability of the feedback loop. Except for above mentioned EEG readout ICs suitable for resistive dry electrodes, several EEG ICs targeting for capacitive dry electrode were developed for better user comfort [63][64]. These ICs feature with ultra-high input impedance to reduce the gain attenuation due to capacitive contact between skin and electrode.

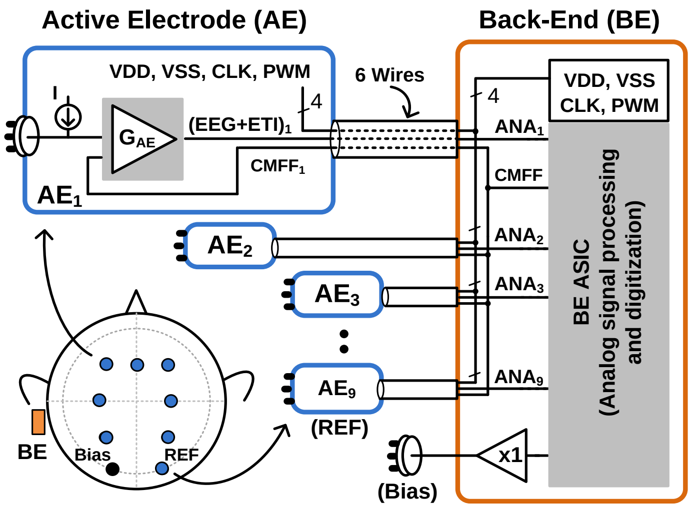

Figure 4.14: 8-channel active-electrode based EEG monitoring system [62]

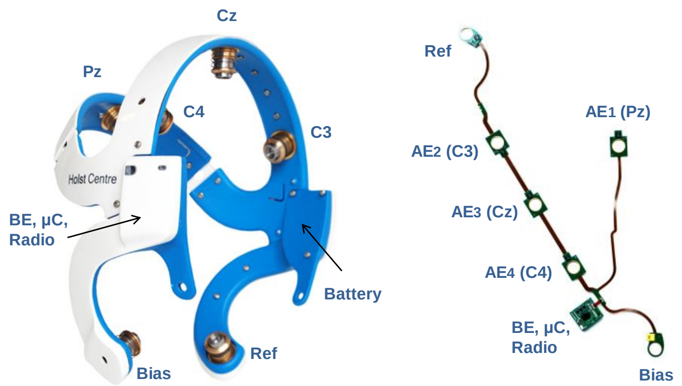

Figure 4.15: imec's wireless EEG headset using active electrodes (combination of gel-free dry electrodes and the recording electronics)

High-quality EEG recording system-on-chip (SoC) with extended sensing modalities and functionalities is the future trend. The combination of conventional analog signal processing and various digital signal processing improve the computing and analysis capability of the ASICs for a wider range of applications. [65] presents a single-chip digital active electrode consists of an analog front-end with a built-in ADC, and an I^2C interface. Each AE can simultaneously monitor biopotential signals, electrode-tissue impedance (ETI) signals, and infra-low frequency (ILF) signals. All active-electrodes can be connected to a generic MCU on the same I^2C bus. The system enables 15-channel biopotential signal acquisition via only 4 wires, significantly reducing system complexity and enabling true modularity. The SoC in [57] integrates amplifier, ADC and digital processor that outputs features-vectors for seizure feature detection. The complete one-channel SoC operates from 1V supply and consumes 9µJ per feature vector. [66] employs an 8-channel analog front-end, a machine-learning seizure classification processor and a 64KB SRAM, showing typical accuracy of 84.4% with 2.03µJ per classification energy efficiency. A lightweight body area network (BAN) [67] consists of network controller IC and sensor node IC was developed for sleep monitoring. It enables the low-power ExG signal acquisition from 14 sensor nodes and low-energy data transmission (0.33pJ/b with data rate of 20Mb/s).

Integrated Circuits for Cardiac Signal Monitoring

In recent year complete cardiac readout ICs have been developed to meet the increasing interest for unobtrusive, ultra-low power, long-term cardiac monitoring devices. A lot of major IC companies now offer dedicated ICs for biomedical signal acquisition and/processing (TI ADS 119x, TI 129x series and Analog devices ADAS100x series)

Figure 4.16 shows for example the block diagram of the TI ADS129x. It features multiple channel readout with integrated analog to digital conversion. In addition to ECG recording, it also supports more advanced functionalities like thoracic impedance measurement (to derive respiration), AC/DC lead-off detection and support for pacemaker pulse detection.

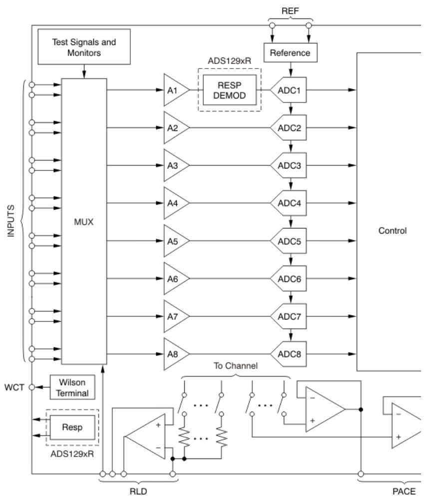

Figure 4.16: Block diagram of TI ADS129x series.

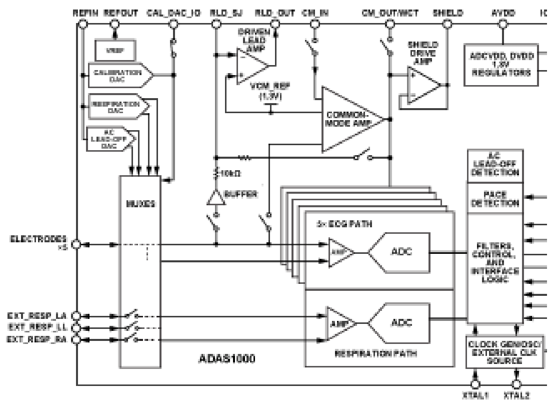

Figure 4.17: Block diagram of ADAS100X series.

Analog devices has a similar offering (see Figure 4.17) with very similar functionalities (multiple parallel channels, integrated analog-to-digital conversion, dedicated respiration path, lead-off detection and pace pulse detection).

In the research area a lot of effort has been spent in recent years on the development of advanced instrumentation amplifier designs. It is well known that the traditional three-opamp architecture (as used in the current commercial IC offerings) doesn't offer the best trade-off in terms of noise and power. Chopper modulation is now widely adopted to reduce the effects of 1/f noise [56]. Other architectures like capacitively coupled [68], or current feedback IAs [69] allow to implement very low-power, high performance ECG readout circuits. By employing very low supply voltage operation, [70] even introduced a 0.09uW ECG amplifier albeit with reduced signal quality performance.

To improve the robustness of ECG recordings under ambulatory conditions, motion artifacts have to be considered carefully. These artifacts can significantly disturb the recording and even saturate the front-end amplifier. [69] introduced concurrent electrode-tissue-impedance measurement, which can be used to estimate certain types of motion artifacts. [71] improved upon this concept by providing real-time active motion artifact suppression (see Figure 4.18) in the analog domain in order to relax the dynamic range requirements.

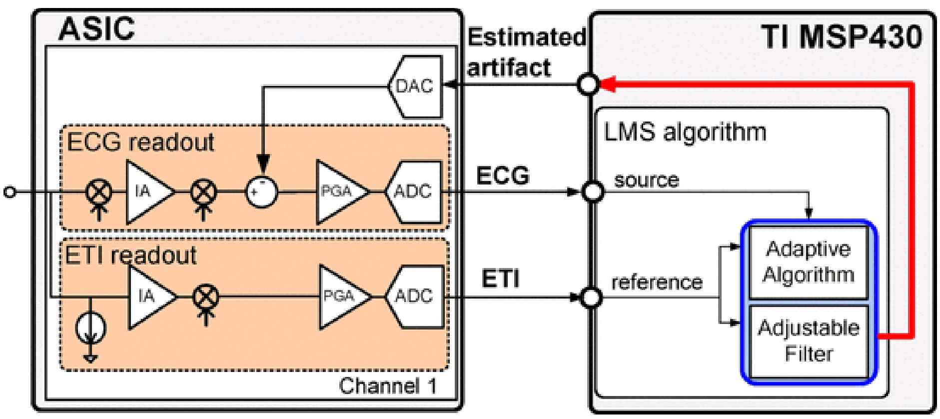

Figure 4.18: Real-time motion artifact suppression introduced by Van Helleputte et al. . [71]

A final trend that has emerged is to build fully integrated systems-on-chip. High-performance analog front-ends are being expanded with integrated wireless transceivers [72][73]. While this has obvious benefits for wearable electronics, the main problem is that too much data has to be wirelessly transmitted. Hence ever more advanced signal processing capabilities are included on the ASICs. This allows doing some local signal processing and only transmitting relevant information. For example [46] introduced an SoC capable of running on-chip heart beat detection algorithms and motion artifact estimation. The complete SoC consumes only 30uW for a heart-beat detection application. [74] demonstrated an SoC employing machine-learning to improve the effectiveness of feature extraction and classification. Also complete wireless SoCs are being shown (i.e. [75]) including analog front-end digital processor and wireless transceiver on a single die.

Traditionally, ECG is being recorded using gel electrodes placed on the chest. While this results in reliable and high-quality signal recordings, it is not the most user friendly and unobtrusive solution. In an effort to reach true unobtrusive ECG recordings, more explorative research is looking into alternative sensing mechanism and locations. One approach is to employ active electrodes or high input impedance potential field probes to enable non-contact ECG measurements [76]. Another approach is looking into dry electrodes possibly integrated into clothing [77].

4.8 Signal Processing

4.8.1 Introduction - Signal processing approaches

Biomedical signal processing covers a rather large domain of application ranging from on-body (accelerometer, ECG, EMG, EOG, …) to in-vivo applications (ENG, spike detection and spike sorting…). Different approaches have been developed in the past to enhance the signal (noise/artifact removal, adaptive filtering), to extract useful information from it (parameter identification using biomechanical model, blind source separation…) in order to deliver useful information to clinicians or system designers.

As a matter of fact, biomedical signal processing is now a mature field that is completely part of most system conception and validation. Furthermore, this processing tends to be performed more and more online on dedicated hardware platforms like DSP or ASIC with a low power budget. This taylors the needs for robust and efficient algorithms in terms of complexity. For instance, cochlear implants are largely using spectral analysis using DSPs to convert audio data into electrical stimulation patterns.

On-line signal processing is useful to reduce the numerical dataflow either using compression algorithms (that takes advantage of signal parsimony in adhoc signal representations) or using advanced feature extraction. EEG-based brain-computer interfaces applications are a good example of the Biomedical signal processing chain value with automatical eye artifact removal, feature computation in temporal/spatial/frequency domain and translation of brain patterns into an effector command using either classification and regression techniques.

Bayesian techniques are now well-established approaches that allow to infer model hyperparameters using priors. These techniques combined with efficient sampling methods are becoming more and more used since they bring additional valuable information on the uncertainty of the estimation. They are now currently used in pattern recognition and parameter identification.

4.8.2 On-line signal processing (on sensor)

Energy-proportional signal processing

In order to realize energy-efficient signal processing for a range of applications and scenarios, signal processing implementations should be energy-performance scalable. Traditional sensing and sensor data analysis however heavily rely on digital signal processing. Typically, the sensed signal is amplified and immediately digitized for analysis through e.g. feature extraction. Under this operating scheme, the power intensive process of signal conditioning and digitization always takes place, regardless of the actual information extracted from the signal later on. Examples of such digital-centric approach can be found in application areas considered, such as sound classification [84][85] and acoustic localization [86], as well as in other wireless sensing applications, such as e.g. biomedical signal sensing and classification [87] and accelerator-based movement analysis [88].

This digital-centric approach fundamentally limits the sensing system's energy-proportionality. Namely, as the signal is always digitized with fixed digitization parameters and further digitally processed, little opportunities for energy-scalability remain. To overcome these limitations, recently 3 trends are emerging to increased sensing and processing system's energy-proportionality:

- *Digital trend*: Hierarchical digital processing: To reduce the fixed energy cost of digital signal processing on a powerful processor when not needing full performance, sensor data processing could be automatically off-loaded to dedicated hardware or a smaller satellite processor when processing simple, frequent tasks. This is e.g. done in Turducken [89] , Somniloquy [90], Little Rock [91], or ARM's big.LITTLE [92]. The technique is often referred to as hierarchical design, or hierarchical processing [93]. Current SotA implementations however do not achieve real energy-proportionality due to 1.) limiting the number of hierarchical tiers to maximum three; 2.) limiting heterogeneity across the hierarchical tiers, which typically each operate in software on a micro-processor; and 3.) using of static, pre-programmed rules to jump from one tier to another.
- *Mixed-signal trend: Adaptive sampling* strategies dynamically reduce a sensor's sampling rate, depending on the information content of the observed signal [94]. Extensions to spatial adaptive sampling [95] adjust the number of active sensor nodes to the correlations of their observed signals with nearby nodes and their own energy budget. This technique however has mostly been applied to low-rate sensor applications, e.g. temperature sensors, while reported gains have typically been below 70%, missing a system-wide, cross-layer coordinated approach.
- *Analog trend*: *Analog feature extraction:* Recently, some implementations start to demonstrate more complex feature extraction in the analog domain, such as analog Mexican hat filtering for ECG analysis [96], sub-band energy and sub-band zero-crossing rate audio feature extraction [97], or even a dedicated glass break sound detection circuitry [98]. Discussed implementations are however static, in the sense that always a fixed set of features is extracted. The systems are not capable of dynamically selecting interesting features, and assign their extraction to the analog, digital, or mixed-signal domain to achieve energy-proportionality.

A drawback of all aforementioned approaches is their inherent limited scaling range due to the localized approach, i.e., scaling is only performance for one sensor and one type of information. Energy-scaling should be enabled across the network (distributed sensing) and also considering multiple types of information (multi-parameter data fusion).

4.8.3 Multi-parameters sensing and data fusion

State of the art

Multi sensing and data fusion are old concepts that gain a new vitality with the ever increasing development of new sensors. Since XXX, there is a tendency to capture more and more physiological signals from a subject in order to have a complete view of its status deliver high-level features to the clinicians (or to the subject itself) and in the future predict its health status.This approach relies on multisensor data collection and multisensor data fusion.

Hardware platforms are developed in research facilities or commercial products to collect data from different sensors using for instance body area networks. Wireless systems are now well established with low-power consumption and high-fidelity RF or UHF transmission. An ubiquitous platform captures both ECG, respiration, temperature and acceleration data. Low-power microcontrollers (TIXXX) or ASICs are used for data conditioning and data acquisition. Some architecture have also been proposed that collect different datatype for onboard processing. IMTEK ASIC relies on impedance and ECG measurements to remove motion-artifact from ECG recordings.

Multi-parametersensing for Ambient Assisted Living

The population of elderly people has been growing rapidly the past decades. Furthermore, studies have shown that elderly people prefer to live in their own dwelling rather than in a nursing home, but often need support to stay independent at home [99]. Postponing a transfer to a nursing home reduces the burden on the healthcare system. Ambient assisted living (AAL) has the aim of enhancing (or maintaining) the quality of life of older people living at home through technology. Enhancing the quality of life can be seen in a broad sense, e.g. fall detection, scheduling daily activities, health/activity monitoring, personal belonging localization, assistance in controlling devices etc.

All these applications require an AAL system to be aware of the environment, hence various sorts of sensors and combinations of sensors have been examined for this purpose. Two groups of sensors are being investigated in this context. The first are the body worn sensors such as accelerometers [100]-[103]. They have a disadvantage of being uncomfortable to wear, easy to forget to put on, and are often not all that useful in an wider variety of applications. The second group consists of the contactless sensors. The usage of cameras has extensively been investigated for AAL systems. Research have been carried out in fall detection [104]-[106], measuring the cardiac pulse rate [107] and in-door tracking [108]. But as concluded in [109] these solutions are often not very robust for real life data. Other sensors such as passive infrared sensors (PIR), radio frequent identification (RFID) tags and various utility sensors have also been investigated but have a poor informative output and are thereby not all that useful on itself for a wider variety of applications. A promising informative sensor signal, in an AAL setup, is that of a microphone [110].

To enable true energy-efficient and reliable operation, all above mentioned sensing approaches should be combined, intelligently, to trade-off energy consumption and sensing performance adaptively.

4.8.4 Distributed algorithms

Distributed signal processing for WBANs and high-density biosensor networks

Wireless body area networks (WBANs) [111][112] provide an answer to the increasing demand for long-term ubiquitous physiological monitoring systems. Similar to body-wide WBANs,one could also envisage the deployment of local mini-scale WBANs

Figure 4.19), which only span a smaller body area (e.g., the head, Figure 4.20), for sensing modalities that rely on high-density sensor arrays, such as electromyography (EMG), electroencephalography (EEG), electrocorticography (ECoG), etc. The modularity of these systems allows for extreme miniaturization (e.g., to replace the bulky EEG headsets that are used nowadays), and a more flexible deployment as nodes can be added/removed/replaced separately.

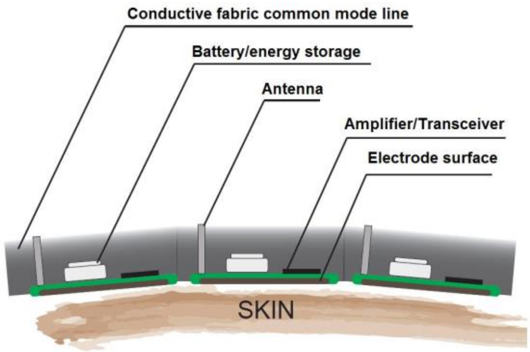

Figure 4.19: Wireless EEG sensor network with common mode line [111]

Increasing the number of sensing nodes or the per-node electrode density, allows more robust recordings with a high spatiotemporal resolution and a wide spatial coverage. However, these systems will then also generate a massive amount of data, such that there will be insufficient transmission energy and computational power to transmit and process all this raw sensor data in real time.

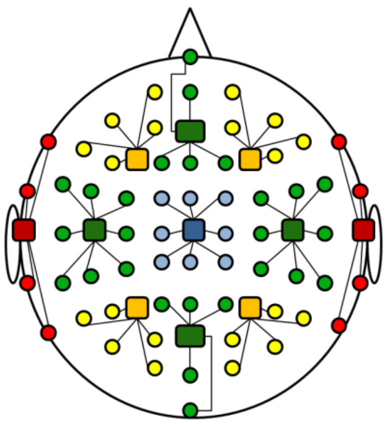

Figure 4.20: Schematic illustration of a hierarchical wireless EEG sensor network [118]

One way to deal with this data deluge is to shift the signal processing (SP) towards the sensing nodes, assuming these nodes are then equipped with a local SP unit. On-chip SP provides a trade-off between computational and wireless transmission energy, as it allows to locally extract and transmit the relevant information instead of the raw data. For example, the on-chip processing in a wireless EEG system has been briefly explored in [113][114]. However, this is typically done on a per-channel basis without exploiting spatial dependency between the electrode signals in an electrode array. This is in conflict with the main goal of high-density arrays, where spatial correlation or spatial filtering is typically an important aspect. For example, spatial correlation is often exploited in EEG signal analysis for, e.g., artifact reduction, source extraction, brain connectivity analysis, detection of event-related potentials, etc.

To exploit spatial correlation in an on-chip processing context, one has to rely on *distributed* SP techniques, in which the local SP tasks at the different nodes are coupled. The nodes then exchange relevant fused signals between each other or with a base station who will then also send feedback to the (other) nodes. Distributed SP algorithm design is highly non-trivial due to the fact that the explicit estimation of the full sensor signal correlation matrix, as used in most multi-channel SP algorithms, inherently requires data centralization. However, if successful, distributed SP techniques may yield a significant reduction in both computational and transmission energy consumption, when compared to their centralized counterparts which require the centralization of raw sensor data, sometimes even without a reduction in estimation accuracy [118] [119]. It is noted that the computational complexity of many (centralized) multi-channel SP algorithms does not scale well with respect to the number of sensors (usually quadratically or worse). This is another reason why distributed SP algorithms are often desirable, i.e., they are highly parallelizable in nature, allowing for multi-core processing strategies.

Although several advances towards the development of WBANs have been made in terms of hardware design, wireless communication link design, and the design of dry and separately deployable (self-attaching) electrodes [111][115][116][117] it appears that the distributed (multi-channel) SP aspects for WBANs have only marginally been addressed [118]. This may result in an increasing gap between hardware and algorithm design, i.e., substantial efforts are required to bridge this gap by means of a close collaboration between both fields.

4.9 References

[1] Simon, E. “Biological and chemical sensors for cancer diagnosis”, (2010) Measurement Science and Technology, 21 (11), art. no. 112002

[2] Veltink, P.H., Bussmann, H.B.J., De Vries, W., Martens, W.L.J., Van Lummel, R.C. Detection of static and dynamic activities using uniaxial accelerometers, (1996) IEEE Transactions on Rehabilitation Engineering, 4 (4), pp. 375-385

[3] Lyons, G.M., Culhane, K.M., Hilton, D., Grace, P.A., Lyons, D. A description of an accelerometer-based mobility monitoring technique, (2005) Medical Engineering and Physics, 27 (6), pp. 497-504

[4] Ghasemzadeh, H., Guenterberg, E., Jafari, R., Energy-efficient information-driven coverage for physical movement monitoring in body sensor networks, (2009) IEEE Journal on Selected Areas in Communications, 27 (1), art. no. 4740886, pp. 58-69

[5] Burchfield, T.R., Venkatesan, S., “Accelerometer-based human abnormal movement detection in wireless sensor networks”, (2007) HealthNet'07: Proceedings of the 1st ACM SIGMOBILE International Workshop on Systems and Networking Support for Healthcare and Assisted Living Environments, pp. 67-69

[6] J. G. Webster, Medical Instrumentation: application and design, 2nd ed. Boston (Mass.): Houghton Mifflin, 1992

[7] Fanget, S., Hentz, S., Puget, P., Arcamone, J., Matheron, M., Colinet, E., Andreucci, P., Duraffourg, L., Meyers, E., Roukes, M.L., Gas sensors based on gravimetric detection - A review, (2011) Sensors and Actuators, B: Chemical, 160 (1), pp. 804-821

[8] Lopez, C.M., Andrei, A., Mitra, S., Welkenhuysen, M., Eberle, W., Bartic, C., Puers, R., Yazicioglu, R.F., Gielen, G.,An implantable 455-active-electrode 52-channel CMOS neural probe,*(2013) Digest of Technical Papers - IEEE International Solid-State Circuits Conference, 56, art. no. 6487738, pp. 288-289*

[9] Robinet, S., Audebert, P., Régis, G., Zongo, B., Beche, J.-F., Condemine, C., Filipe, S., Charvet, G., A low-power 0.7 μv rms 32-channel mixed-signal circuit for ECoG recordings,*(2011) IEEE Journal on Emerging and Selected Topics in Circuits and Systems, 1 (4), art. no. 6133298, pp. 451-460*

[10] B. Murmann, "ADC Performance Survey 1997-2013," [Online]. Available: http://www.stanford.edu/~murmann/adcsurvey.html

[11] Renard, S., Pisella, C., Collet, J., Perruchot, F., Kergueris, C., Destrez, P., Rey, P., (...), Dallard, E., Miniature pressure acquisition microsystem for wireless in-vivo measurements, (2000) Proc. IEEE-EMBS, pp. 184-187

[12] G. Jourdan, E. Colinet, J. Arcamone, A. Niel, C. Marcoux, L. Duraffourg, NEMS-based heterodyne self-oscillator, Sensors and Actuators A: Physical, Volume 189, 15 January 2013, Pages 512-518

[13] Ayazian, S., Akhavan, V. A., Soenen, E., & Hassibi, A. (2012). A photovoltaic-driven and energy-autonomous CMOS implantable sensor. *Biomedical Circuits and Systems, IEEE Transactions on*, *6*(4), 336-343.

[14] Kerzenmacher, S., Ducrée, J., Zengerle, R., & Von Stetten, F. (2008). Energy harvesting by implantable abiotically catalyzed glucose fuel cells. *Journal of Power Sources*, *182*(1), 1-17..

[15] J.F; Christmann, E. Beigné, C. Condemine, N. Leblond, P. Vivet, G. Waltisperger, J. Wilemin " Bringing Robustness and Power Effiiency to Autonomous Energy Harvesting Microsystems", IEEE Symposium in Asynchronous Circuits and Systems, 2010, pp 62-71

[16] R. Ramezani, A. Yakovlev, T. Mak, D. Shang " Voltage Sensing Using an Asynchronous Charge-To-Digital Converter for Energy Harvesting Circuits", Technical Report NCL-EECE-MSD-TR-20120-160, October 2010, Newcastle University.

[17] Kim, S., Yan, L., Mitra, S., Osawa, M., Harada, Y., Tamiya, K., Van Hoof, C., Yazicioglu, R.F., A 20μW intra-cardiac signal-processing IC with 82dB bio-impedance measurement dynamic range and analog feature extraction for ventricular fibrillation detection, *(2013) Digest of Technical Papers - IEEE International Solid-State Circuits Conference, 56, art. no. 6487745, pp. 302-303*

[18] B. Rumberg, D.W. Graham, and V. Kulathumani "Hibernets: energy-efficient sensor networks using analog signal processing", Proceedings othe 9th ACM/IEEE Conference on Information Processing in Sensor Networks , 2010, pp 129-139

[19] C. Weltin-Wu, Y. Tsividis "An Event-Driven Clockless Level-Crossing ADC With Signal-Dependent Adaptive Resolution", IEEE Journal of Solid State Ciircuits, Vol 48, N° 49, September 2013,

[20] H. Kim, C. Van Hoof, R. Yazicioglu " A Mixed Signal ECG Processing Platform with an adaptive Sampling ADC for Portable Monitoring Applications", 33rd IEEE International Conference of EMBS, 2011, pp 2196-2199

[21] M. Zaare, H. Sepehrian, M. Maymandi-Nejad " A new non-uniform adaptive-sampling successive approximation ADC for biomedical sparse signals", Analog Integrated Circuit Signal processing Journal, Springer, 7 December 2012

[22] Lee, J., Rhew, H. G., Kipke, D. R., & Flynn, M. P. (2010). A 64 channel programmable closed-loop neurostimulator with 8 channel neural amplifier and logarithmic ADC. *Solid-State Circuits, IEEE Journal of*, *45*(9), 1935-1945.

[23] Schuster, C., Nagel, J.L., Piguet, C., Farine, P.A., "Architectural and technology influence on the optimal total power consumption". DATE 2006: 989-994

[24] Ickes, N., Y. Sinangil, F. Pappalardo, E. Guidetti, A. P. Chandrakasan, "A 10 pJ/cycle ultra-low-voltage 32-bit microprocessor system-on-chip," ESSCIRC 2011 pp.159-162, 12-16 Sept. 2011

[25] Konijnenburg, M.; Yeongojn Cho; Ashouei, M.; Gemmeke, T.; Changmoo Kim; Hulzink, J.; Stuyt, J.; Mookyung Jung; Huisken, J.; Soojung Ryu; Jungwook Kim; de Groot, H., "Reliable and energy-efficient 1MHz 0.4V dynamically reconfigurable SoC for ExG applications in 40nm LP CMOS," ISSCC 2013, pp.430,431, 17-21

[26] Vincent, L., Maurine, P., Lesecq, S., Beigné, E., "Embedding statistical tests for on-chip dynamic voltage and temperature monitoring", 2012, Design Automation Conference , pp. 994-999

[27] Rebaud, B., Belleville, M., Beigné, E., Bernard, C., Robert, M., Maurine, P., Azemard, N., "Timing slack monitoring under process and environmental variations: Application to a DSP performance optimization", 2011, Microelectronics Journal 42 (5) , pp. 718-732

[28] J.-L. Nagel, C. Arm, A. Corbaz, M. Morgan, V. Moser, P. Volet, "The icyflex4 Processor, a Scalable DSP Architecture", CSEM Scientific and Technical Report 2009

[29] Novo, D.; Kritikakou, A.; Raghavan, P.; Van der Perre, L.; Huisken, J.; Catthoor, F., "Ultra low energy Domain Specific Instruction-set Processor for on-line surveillance," Application Specific Processors (SASP), 2010 IEEE 8th Symposium on , pp.30,35, 13-14 June 2010

[30] Berder, O., Sentieys, O., PowWow: Power Optimized Hardware/Software Framework for Wireless Motes, Workshop on Ultra-Low Power Sensor Networks (WUPS), co-located with Int. Conf. on Architecture of Computing Systems (ARCS 2010), 2010, pp.229-233

[31] http://www.arm.com/products/processors/technologies/biglittleprocessing.php

[32] Tovinakere Dwarakanath, V., "Ultra-Low Power Reconfigurable Architectures for Controllers in Wireless Sensor Network Nodes", Thesis, Rennes 1 University, 2013

[33] Jiawei Huang; Lach, J., "Exploring the fidelity-efficiency design space using imprecise arithmetic," Design Automation Conference (ASP-DAC), 2011 16th Asia and South Pacific, pp.579, 584, 25-28 Jan. 2011

[34] Lingamneni, A., Enz, C., Palem, K. Piguet, C., "Designing Energy-Efficient Arithmetic Operators Using Inexact Computing", Journal of Low Power Electronics, Volume 9, Number 1, April 2013, pp. 141-153(13)

[35] http://www.tiempo-ic.com/products/ip-cores/TAM16.html

[36] Coppa, B., Heliot, R., Michel, O., Moisan, E. & David, D., "Low-cost intracortical spiking recordings compression with classification abilities for implanted BMI devices", Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS 2012, pp. 2623.

[37] Kanoun, K.; Mamaghanian, H.; Khaled, N.; Atienza, D., "A real-time compressed sensing-based personal electrocardiogram monitoring system," Design, Automation & Test in Europe Conference & Exhibition (DATE), 2011, pp.1, 6, 14-18 March 2011

[38] Gosselin, Benoit. 2011. "Recent Advances in Neural Recording Microsystems." *Sensors* 11, no. 5: 4572-4597.

[39] Harrison, R.R., "The Design of Integrated Circuits to Observe Brain Activity," Proceedings of the IEEE et al. "A low-power low-noise CMOS amplifier for neural recording applications," JSSC, vol.9638, no.76, pp.1203,1216, July 2008.

[40] Gosselin, B.; Ayoub, A.E.; Roy, J.-F.; Sawan, M.; Lepore, F.; Chaudhuri, A.; Guitton, D., "A Mixed-Signal Multichip Neural Recording Interface With Bandwidth Reduction," Biomedical Circuits and Systems, IEEE Transactions on , vol.3, no.3, pp.129,141958, 965, June 2009.2003

[41] Moo-Sung Chae; Yang, Zhi; Yuce, M.R.; Linh Hoang; Wentai Liu, "A 128-Channel 6 mW Wireless Neural Recording IC With Spike Feature Extraction and UWB Transmitter," Neural Systems and Rehabilitation Engineering, IEEE Transactions on , vol.17, no.4, pp.312,321, Aug. 2009.

[42] Shahrokhi, F.; Abdelhalim, Karim; Serletis, D.; Carlen, P.L.; Genov, R., "The 128-Channel Fully Differential Digital Integrated Neural Recording and Stimulation Interface," Biomedical Circuits and Systems, IEEE Transactions on , vol.4, no.3, pp.149,161, June 2010.

[43] Sodagar, A.M.; Perlin, G.E.; Ying Yao; Najafi, K.; Wise, K.D., "An Implantable 64-Channel Wireless Microsystem for Single-Unit Neural RecordingYaziciogluRecording

[44] YaziciogluRecordingYazicioglu et al., "A 60uW 60nV/rtHz Readout Front-End for Portable Biopotential Acquisition Systems," ISSC Digest of Technical Papers 2006, paper 2.6, Feb. 2006.

[45] Muller, R.; Gambini, S.; Rabaey, J.M., "A 0.013mm2 5μW DC-coupled neural signal acquisition IC with 0.5V supply," Solid-State Circuits, Conference Digest of Technical Papers (ISSCC), 2011 IEEE International , vol., no., pp.302,304, 20-24 Feb. 2011

[46] Hyejung Kim, Yazicioglu, R.F., Sunyoung Kim, Van Helleputte, N., Artes, A., Konijnenburg, M., Huisken, J., Penders, J., Van Hoof, C., A configurable and low-power mixed signal SoC for portable ECG monitoring applications (2011), Symposium on VLSI Circuits (VLSIC), pp.142 – 143

[47] Jeon, D., Seok, M., Chakrabarti, C., Blaauw, D. and Sylvester, D., A super-pipelined Energy Efficient Subthreshold 240MS/s FFT core in 65 nm CMOS, (2012) IEEE Journal of , vol.44, no.9, pp.2591,2604, Sept. 2009Solid-State Circuits, 47, pp.23-34, 2012.

[48] Hua Gao; Walker, R.M.; Nuyujukian, P.; Makinwa, K. A A; Shenoy, K.V.; Murmann, B.; Meng, T.H., "HermesE: A 96-Channel Full Data Rate Direct Neural Interface in 0.13 μm CMOS," Solid-State Circuits, IEEE Journal of , vol.47, no.4, pp.1043,1055, April 2012

[49] Biederman, W.; Yeager, D.J.; Narevsky, N.; Koralek, A.C.; Carmena, J.M.; Alon, E.; Rabaey, J.M., "A Fully-Integrated, Miniaturized (0.125 mm^2) 10.5 μW Wireless Neural Sensor," Solid-State Circuits, IEEE Journal of , vol.48, no.4, pp.960,970, April 2013.

[50] Lopez, C.M.; Andrei, A.; Mitra, S.; Welkenhuysen, M.; Eberle, W.; Bartic, C.; Puers, R.; Yazicioglu, R.F.; Gielen, G., "An Implantable 455-Active-Electrode 52-Channel CMOS Neural Probe," Solid-State Circuits, IEEE Journal of , vol., no., pp., Jan. 2014.

[51] Tung-Chien Chen, Kuanfu Chen, Zhi Yang, Cockerham, K., Wentai Liu (2009), A biomedical multiprocessor SoC for closed-loop neuroprosthetic applications, IEEE International Solid-State Circuits Conference (ISSCC), pp.434 - 435,435

[52] R. R. Harrison and C. Charles, "A Low-Power Low-Noise CMOS Amplifier for Neural Recording Applications," *IEEE J. Solid-State Circuits*, pp. 958-965, June 2003.

[53] W. Wattanapanitch, M. Fee, and R. Sarpeshkar, "An energy-efficient micropower neural recording amplifier," *IEEE Trans. Biomedical Circuits Syst*., vol. 1, pp. 136–147, 2007.

[54] H. Wu, Y. Xu., "A 1V 2.3μW Biomedical Signal Acquisition IC," *ISSCC* Dig. Tech. Papers, pp. 119-128, 2006.

[55] X. Zou, W. S. Liew, L. Yao and Y. Lian, "A 1-V 22-μW 32-Channel Implantable EEG Recording IC," *ISSCC* Dig. Tech. Papers, pp. 126-128, 2010.

[56] T. Denison, K. Consoer, A. Kelly et al., "A 2.2μW 94nV/√Hz, Chopper-Stabilized Instrumentation Amplifier for EEG Detection in Chronic Implants," *ISSCC* Dig. Tech. Papers, pp. 162-594, 2007.

[57] N. Verma, A. Shoeb, A. J. Bohorquez et al., "A Micro-Power EEG Acquisition SoC With Integrated Feature Extraction Processor for a Chronic Seizure Detection System," *IEEE J. Solid-State Circuits*, pp. 804-816, April 2010.

[58] R. F. Yazicioglu, P. Merken, R. Puers, C. Van Hoof. "A 200 uW eight-channel EEG acquisition ASIC for ambulatory EEG systems". *IEEE J. Solid-State Circuits*. pp. 3025–3038, Dec 2008.

[59] T. Degen, S. Torrent, H. Jackel., "Low-Noise Two-Wired Buffer Electrodes for Bioelectric Amplifiers," *IEEE Trans on Biomed Eng*. vol. 54, pp. 1328 – 1332, 2007.

[60] J. Xu, R. F. Yazicioglu, P. Harpe, K.A.A. Makinwa, C. Van Hoof, "A 160μW 8-channel active electrode system for EEG monitoring," ISSCC Dig. Tech. Papers, pp. 300-302, 2011.

[61] M. Guermandi, R. Cardu, E. Franchi, R. Guerrieri, "Active electrode IC combining EEG, electrical impedance tomography, continuous contact impedance measurement and power supply on a single wire," Proc of ESSCIRC, pp.335,338, 12-16 Sept. 2011.

[62] S. Mitra, J. Xu, A. Matsumoto, K.A.A Makinwa, C. Van Hoof, R. F. Yazicioglu, "A 700μW 8-channel EEG/contact-impedance acquisition system for dry-electrodes", Symposium on VLSI Circuits (VLSIC), pp. 68-69, June, 2012.

[63] Y.M. Chi, C. Maier, G. Cauwenberghs "Integrated ultra-high impedance front-end for non-contact biopotential sensing" IEEE Journal of Emerging and Selected Topics in Circuits and Systems, pp.526-535, Dec 2011.

[64] R. Matthews, N. McDonald et al., "The invisible electrode-zero prep time, ultra low capacitive sensing". Proceedings of the *11th International Conference on HumanComputer Interaction (2005).*

[65] J. Xu, B. Büsze, H. Kim, K.A.A Makinwa, C. Van Hoof, R.F.Yazicioglu "A 60nV/rt(Hz) 15-Channel Digital Active Electrode System for Portable Biopotential Signal Acquisition" to appear in ISSCC 2014.

[66] Jerald Yoo, Long Yan, Dina El-Damak, Muhammad Awais Bin Altaf, Ali H. Shoeb, and Anantha P. Chandrakasan, "An 8-channel Scalable EEG Acquisition SoC with Patient-Specific Seizure Classification and Recording Processor" *IEEE Journal of Solid-State Circuits (JSSC),* pp. 214-228, vol. 48, no. 1, Jan. 2013.

[67] S. Lee, L. Yan, T. Roh, S. Hong, amd H.-J. Yoo., "A 75μW real-time scalable body areanetwork controller and a 25μW ExG sensorIC for compact sleep monitoring applications,"IEEE J. Solid-State Circuits, vol. 47,no. 1, pp. 323–334, Jan. 2012.

[68] Qinwen Fan, et al., "A 1.8 uW 60 nV/√Hz Capacitively-Coupled Chopper Instrumentation Amplifier in 65 nm CMOSR. Harrison, "A low-power integrated circuit for adaptive detectionWireless Sensor Nodes," *IEEE Journal of Solid-State Circuits*, vol.46, no.7, pp.1534-1543, July 2011

[69] Yazicioglu, R.F.; Sunyoung Kim; Torfs, T.; Hyejung Kim; Van Hoof, C., "A 30 uW Analog Signal Processor ASIC for Portable Biopotential Signal Monitoring," *Solid-State Circuits, IEEE Journal*action potentials in noisy signals," in Proceedings *of* , vol.46, no.1, pp.209,223, Jan. 2011

[70] Yuhwai Tseng; Yingchieh Ho; Shuoting Kao; Chauchin Su, "A 0.09 μW Low Power Front-End Biopotential Amplifier for Biosignal Recording," *Biomedical Circuits and Systems, IEEE Transactions on* , vol.6, no.5, pp.508,516, Oct. 2012

[71] Van Helleputte, N.; Sunyoung Kim; Hyejung Kim; Jong Pal Kim; Van Hoof, C.; Yazicioglu, R.F., "A 160 uABiopotential Acquisition IC With Fully Integrated IA and Motion Artifact Suppression," *Biomedical Circuits and Systems, IEEE Transactions on* , vol.6, no.6, pp.552,561, Dec. 2012

[72] Tee Hui Teo; Xinbo Qian; Kumar Gopalakrishnan, P.; Hwan, Y.S.; Haridas, Kuruveettil; Chin Yann Pang; Hyouk-Kyu Cha; Minkyu Je, "A 700- μW Wireless Sensor Node SoC for Continuous Real-Time Health Monitoring," *Solid-State Circuits, IEEE Journal of* , vol.45, no.11, pp.2292,2299, Nov. 2010

[73] Khayatzadeh, M.; Xiaoyang Zhang; Jun Tan; Wen-Sin Liew; Yong Lian, "A 0.7-V 17.4-/spl mu/W 3-Lead Wireless ECG SoC," *Biomedical Circuits and Systems, IEEE Transactions on* , vol.7, no.5, pp.583,592, Oct. 2013

[74] Shu-Yu Hsu; Yingchieh Ho; Po-Yao Chang; Pei-Yu Hsu; Chien-Ying Yu; Yuhwai Tseng; Tze-Zheng Yang; Ten-Fang Yang; Chen, R.-J.; Chauchin Su; Chen-Yi Lee, "A 48.6-to-105.2μW machine-learning assisted cardiac sensor SoC for mobile healthcare monitoring," *VLSI Circuits (VLSIC), 2013 Symposium on* , vol., no., pp.C252,C253, 12-14 June 2013

[75] Shu-Yu Hsu; Yingchieh Ho; Yuhwai Tseng; Ting-You Lin; Po-Yao Chang; Jen-Wei Lee; Ju-Hung Hsiao; Siou-Ming Chuang; Tze-Zheng Yang; Po-Chun Liu; Ten-Fang Yang; Ray-Jade Chen; Chauchin Su; Chen-Yi Lee, "A sub-100μW multi-functional cardiac signal processor for mobile healthcare applications," *VLSI Circuits (VLSIC), 2012 Symposium on* , vol., no., pp.156,157, 13-15 June 2012

[76] the 25thGuoChen Peng; Bocko, M.F., "A low noise, non-contact capacitive cardiac sensor," *Engineering in Medicine and Biology Society (EMBC), 2012 Annual International Conference of the IEEE* , vol., no., pp.4994,4997, Aug. 28 2012-Sept. 1 2012

[77] Long Yan; Yoo, J.; Binhee Kim; Hoi-Jun Yoo, "A 0.5- uVrms, 12- uW Wirelessly Powered Patch-Type Healthcare Sensor for Wearable Body Sensor Network," *Solid-State Circuits, IEEE Journal of* , vol.45, no.11, pp.2356,2365, Nov. 2010

[78] R. Harrison, "A low-power integrated circuit for adaptive detection of action potentials in noisy signals," in Proceedings of the 25th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Cancun, Mexico, 2003.

[79] B. Gosselin and M. Sawan, "An Ultra Low-Power CMOS Automatic Action Potential Detector," IEEE Transactions on Neural Systems and Rehabilitation Engineering, vol. 17, no. 4, pp. 346 - 353, Aug. 2009.

[80] R. Sarpeshkar, "Analog Versus Digital: Extrapolating from Electronics to Neurobiology," Neural Computation, Boston, 1998.

[81] M. Shoaib, "Design of Energy-efficient Sensing Systems with Direct Computations on Compressively-sensed Data," Princeton University, New Jersy, September 2013.

[82] P. K. Baheti and H. Garudadri, "An Ultra Low Power Pulse Oximeter Sensor Based on Compressed Sensing," in Sixth International Workshop on Wearable and Implantable Body Sensor Networks, 2009. BSN 2009, Berkeley, CA, 3-5 June 2009.

[83] Kyong Ho Lee, Naveen Verma (2013), A Low-Power Processor With Configurable Embedded Machine-Learning Accelerators for High-Order and Adaptive Analysis of Medical-Sensor Signals, IEEE Journal of Solid-state Circuits, 48 (7), pp.1625-1637

[84] E. Alexandre et al., Audio Engineering Society Convention, 2009.

[85] Feki, et al., International Conference on Multimedia Computing and Systems, 2011.

[86] Wang H, Chen CE, Ali A, et al; “Acoustic sensor networks for woodpecker localization,” Optics & Photonics, 2005.

[87] H. Kim et al., Synopsium on VLSI Circuits, 2011.

[88] Yang, C.-C.; Hsu, Y.-L., “A Review of Accelerometry-Based Wearable Motion Detectors for Physical Activity Monitoring,” Sensors 2010, 10, 7772-7788.

[89] Sorber, Jacob, et al. "Turducken: hierarchical power management for mobile devices." Proceedings of the 3rd international conference on Mobile systems, applications, and services. ACM, 2005.

[90] Agarwal, Yuvraj, et al. "Somniloquy: augmenting network interfaces to reduce PC energy usage." Proceedings of the 6th USENIX symposium on Networked systems design and implementation. USENIX Association, 2009..

[91] B. Priyantha, D. Lymberopoulos, and J. Liu, "Little Rock: Enabling Energy Efficient Continuous Sensing on Mobile Phones," Microsoft Research, tech. rep. MSR-TR- 2010-14, 2010.

[92] ARM. (2011) big.LITTLE Processing with the Cortex-A15 and Cortex-A7 Processors. [Online] http://www.arm.com

[93] D. Raskovic, Ph.D. thesis, "Energy-efficient Hierarchical Processing in the Network of Wireless Intelligent Sensors (WISE),""University of Alabama in Huntsville, AL, 2003.

[94] E. C.-H. Ngai, J. L. Z. Ruan, "Wireless sensor deployment for collaborative sensing with mobile phones," The International Journal of Computer and Telecommunications Networking, vol. 55, no. 15, 2011.

[95] V. Raghunathan, S. Ganeriwal, and M. Srivastava, "Emerging techniques for long lived wireless sensor networks," IEEE Communications Magazine, vol. 44, no. 4, pp. 108 - 114, 2006.

[96] Singh, A.; Yazicioglu, R.F.; Van Hoof, C.; , "Design of widely tunable Mexican hat wavelet filter for cardiac signal analysis," Circuits and Systems (ISCAS), 2011 IEEE International Symposium on , vol., no., pp.1459-1462, 15-18 May 2011

[97] Leung Kin Chiu; Gestner, B.; Anderson, D.V., "Design of analog audio classifiers with AdaBoost-Based feature selection," Circuits and Systems (ISCAS), 2011 IEEE International Symposium on , vol., no., pp.2469-2472, 15-18 May 2011.

[98] Gestner, B.; Tanner, J.; Anderson, D., "Glass Break Detector Analog Front-End Using Novel Classifier Circuit," Circuits and Systems, 2007. ISCAS 2007. IEEE International Symposium on , vol., no., pp.3586-3589, 27-30 May 2007.

[99] Counsel and Care, Community care assessment and services, April, 2005.

[100] Prado, M.J. Reina-Tosina and L Roa, "Distributed intelligent architecture for falling detection and physical activity analysis in the elderly", in Proceedings of the second Joint EMBS/BMES conference. 2002. Houston, TX, USA. October 23-26, 2002.

[101] Díaz, A. et al. "Preliminary evaluation of a full-time falling monitor for the elderly" in Proceedings of the 26th Annual International Conference of the IEEE-EMBS, San Francisco, CA, USA. September 1-5, 2004.

[102] Bourke, J. O'Brien and G. Lyons , "Evaluation of a threshold-based tri-axial accelerometer fall detection algorithm" Gait Posture, 2006.

[103] Bourke AK, GM Lyons, "A threshold-based detection algorithm using a bi-axial gyroscope sensor", Med. Eng. Phys., 2006.

[104] Wu G., "Distinguishing fall activities from normal activities by velocity characteristics", Jour. of Biomechanics, 33, pp.1497-1500, 2000.

[105] Nait-Charif, H. and S Mckenna "Activity Summarisation and Fall Detection in a Supportive Home Environment". in 17th International Conference on Pattern Recognition, 2004.

[106] Mihailidis A. "An intelligent emergency response system: preliminary development and testing of automated fall detection" , J. Telemed. Telecare;11(4):194-8, 2005.

[107] [ ] M. Z. Poh, D. J. McDuff, and R. W. Picard. Noncontact, automated cardiac pulse measurements using video imaging and blind source separation. Opt. Express, 18(10):10762–10774, May 2010.

[108] Mihailidis, T. Tam, M. McLean, and T. Lee. An intelligent health monitoring and emergency response system. In Proc. International Conference on Smart Homes and Health Telematics (ICOST), pages 272–281, 2005.

[109] Fabien, Cardinaux, Deepayan , Bhowmik, Charith, Abhayaratne and Mark S., Hawley. Video Based Technology for Ambient Assisted Living: A review of the literature. Journal of Ambient Intelligence and Smart Environments (JAISE) . ISSN 1876-1364. 2011.

[110] M. Vacher et al, Development of Audio Sensing Technology for Ambient Assisted Living: Applications and Challenges, International Journal of E-Health and Medical Communications, 2(1), p35-54, 2011.

[111] Y. Chi, S. Deiss, and G. Cauwenberghs, "Non-contact low-power EEG/ECG electrode for high density wearable biopotential sensor networks," in International Workshop on Wearable and Implantable Body Sensor Networks, 2009, pp. 246–250.

[112] M.-F. Wu and C.-Y. Wen, “Distributed cooperative sensing scheme for wireless sleep EEG measurement,” IEEE Sensors Journal, vol. 12, no. 6, pp. 2035–2047, 2012.
[113] A. Casson, D. Yates, S. Smith, J. Duncan, and E. Rodriguez-Villegas, “Wearable electroencephalography,” IEEE Engineering in Medicine and Biology Magazine, vol. 29, no. 3, pp. 44–56, 2010.
[114] N. Verma, A. Shoeb, J. V. Guttag, and A. Chandrakasan, “A micro-power EEG acquisition soc with integrated seizure detection processor for continuous patient monitoring,” in Symposium on VLSI Circuits, 2009, pp. 62–63.
[115] M. Sun,W. Jia,W. Liang, and R. Sclabassi, “A low-impedance, skin-grabbing, and gel-free EEG electrode,” in International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), 2012, pp. 1992–1995.
[116] T. Someya, “Building bionic skin,” IEEE Spectrum, vol. 50, no. 9, pp. 44–49, 2013.
[117] . R. Ives, “New chronic EEG electrode for critical/intensive care unit monitoring,” Journal of Clinical Neurophysiology, vol. 22, no. 2, pp. 119–123, April.
[118] A. Bertrand and M. Moonen, "Distributed eye blink artifact removal in a wireless EEG sensor network", Internal Report KU Leuven ESAT/STADIUS, 2013.
[119] A. Bertrand and M. Moonen, "Distributed adaptive node-specific signal estimation in fully connected sensor networks - Part I: sequential node updating", IEEE Transactions on Signal Processing, vol. 58, no.10, pp. 5277 - 5291, 2010.

Chapter 5 Integration and Packaging

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5.1 Introduction

Today's wearable and implantable medical devices are often complex systems, based on advanced electronics (mixed-signal front-ends, DSP, transceiver, power management, memory, …). Nevertheless, they predominantly rely on rather traditional system design and technology for integration and packaging. The electronic subsystem of these devices is assembled using conventional board-level and/or package-level integration. Although this has enabled a variety of diagnostic and therapeutic applications, the achievable miniaturization remained limited due to the chosen conventional integration technology. The use of advanced 2D and 3D integration technologies such as those being developed for nano-electronics integrated circuit applications will enable a drastic further miniaturization of the electronic subsystem of these devices. It will also improve yield, testability and cost effectiveness. Alternatively, if this reduction in size is not essential, it will free space for additional system functionality (such as sensing or actuation).

5.2 SoC vs SiP

For decades the development of IC technologies is oriented towards SoC (System on Chip) as the ultimate dream. Despite the huge technological challenges, the technology scaling as driven by Moore's Law and the ITRS roadmaps still forecasts increasing performance and functionality (complexity) at decreasing cost. This evolution is very attractive for electronic systems in many application domains: the steep rise of personal computers and telecommunication devices (mobile phones, tablets…) is largely enabled by this technology explosion. All applications where complex functions are required are affected, so also smart healthcare devices take advantage of this evolution.

System integration solutions for smart healthcare systems typically have to meet several specific requirements: these systems have to be light weight, have a very thin and often a flexible embodiment to allow comfortable wearing and they have to operate at very low power levels (due to battery lifetime limitations). Devices are often worn in contact to the skin (hypo allergic materials) or even implanted, this adds severe package material requirements and dedicated technologies that can counter these challenges.

The electronic part of these medical systems can be implemented in various ways: using the unique properties of the CMOS scaling revolution over the last 40 years, very powerful and complex electronic systems can be realized on a single chip, allowing to reduce cost, size and power combined with high performing behavior. SoC (System on Chip) solutions are intrinsically complex, highly integrated single Silicon chip systems, sometimes combined with some analog functionality (e.g. A/D convertors, opamps, drivers…). Such systems exploit fully the Moore's law driven technology development following e.g. the ITRS roadmaps. In this way, very cost effective systems are built. But these smart systems increasingly require a wide range of very different functions: optical sensors (e.g. imager devices), acoustic transducers, power devices, RF devices and components etc. often need to be combined. Adding additional functionality however requires often the use of alternative technologies which are hard to combine on the same chip, especially when more than one extra function is required. An interesting example (among others) is an approach where post-processing of SiGe layers on standard advanced CMOS is used to integrate monolithically additional mechanical (MEMS) functionality: accelerometer, gyroscope, magnetometer, microphone, pressure sensor,… are enabled with this technology (see[1])

In [2] an ultrasound scanning device system with integrated CMUTs (Capacitive Micromachined Ultrasound Transducers) is developed showing how far integrated technologies can impact SoCs. But further adding RF transducers (for e.g. wireless communication with a handheld device) and antennes make such a system too large and too expensive at even reduced performance.

Therefore the SiP approach offers adequate solutions: combine circuits, devices and components in a smart way such that first the SoC advantages are exploited and use interposer technologies (on Si, flex, stretch…) to connect these multiple devices in the required shape. (See example in ecubes – www.ecubes.org - with healthcare module).

In Table 5.2 a summary of important advantages and disadvantages of the 2 approaches is list

Table 5.2: Summary of important pro's and con's for SoC versus SiP integration strategy

SoC	SiP
+ Robust design flow – EDA and system design available	- Limited design flow integration
+ Small footprint	- Larger modules due to the use of interposer, limited interconnect density capability
+ Low cost mass production	- Interposer/package cost
+ Monolithic process reduces assembly and testing costs in large volumes	- Testing of many individual components (KGD) required to avoid high compound yield loss
- Larger die and heterogeneous technology (e.g. postprocessing) increases die cost	+ Wide variety of technologies available in the packaging and assembly supply chain.
- Monolithic processing requires a comprise in performance between the different integrated functions	+ Flexibility: allows to mix-and-match technologies, reuse of existing components and integration of non-Si components
- CMOS scaling more-and-more diverging from e.g. analog and memory scaling	+ Optimized performance of each function (towards, cost, power consumption..)
- Restricted to Si-based integration (and compatible technologies)	+ Use most effective component technology (MEMS, III-V,…)

From this table it is obvious that there is no single winning technological approach: system designers will have to optimize and combine both approaches in such a way that the solution developed meets the application requirements in cost, form factor and technical performance. Subsequently a thorough understanding of a wide variety of packaging and integration techniques is always needed.

5.3 Flexible chip and system packaging

5.3.1 Wafer thinning

In its latest report on thin wafers and temporary bonding [1], Yole Développement predicts that by 2017, 74 % of all wafers will have a thickness of less than 100 µm. Driving applications for ultra-thin wafers, with a thickness below 40 µm, are memory stacking for increased functional density and power components for improved thermal management. Flexible chip packaging also reaps the benefits of this drive towards extremely thin chips.

The most renowned technology for manufacturing ultra-thin chips with thickness below 50 µm is based on a multi-stage back grinding process [4]. Silicon wafers with standard thickness in the range of 500-800 µm undergo first a coarse back grinding to reach an intermediate thickness of 100-200 µm. At this stage, a more sophisticated micro-thinning process (i.e. CMP, fine grinding, plasma etching or wet etching) is used to remove additional material as well as to eliminate the defects and stress resulting from the coarse grinding process, allowing the wafer to be ground to less than 50 µm thickness. The necessary follow-up processes such as the removal of the protective film or dicing, are difficult to control. One approach that is reducing the undesired edge chipping during chip dicing, as well as minimizing the yield loss during subsequent processing steps is the 'Dicing Before Grinding' (DBG) technique [5]. Here, trenches with a cutting depth larger than the desired final chip thickness are sawn on the wafer front side prior to the back grinding process. After gluing the front side of the partial diced wafer on a carrier foil and thinning at the backside to the desired chip thickness, the chips are completely singulated and ready to pick from the foil.

This DBG and subsequent thinning technology is well developed and is widely used within industry for the production of chips with thicknesses down to 40 µm. For flexible electronics however, this thickness is not sufficient. Only at thicknesses around 25 µm, the chip becomes sufficiently flexible to be suitable for the reliable usage in flexible electronics. Even applications that do not require extreme bending radii benefit from the use of ultra-thin chips, as for example the comfort of wearable patches improves dramatically with increased flexibility and reduced weight. Some exploratory work has been performed using chip thicknesses below 40 µm [6],[7].

In recent years, alternative methods for producing ultra-thin chips have emerged, overcoming some of the drawbacks of back grinding (subsurface damage, induced stress). Examples are the IMS Chipfilm™ technology [8], where CMOS chips are realized in an epitaxial grown silicon layer on top of a porous silicon layer, or the CIRCONFLEX technology from Philips [9]. While these technologies differ strongly in the way the thin chips are realized, they all result in an increased mechanical strength of the ultra-thin chips, making it possible to reach bending radii down to 0.5 mm. The reduction of induced stress is of specific interest for manufacturing ultra-thin and highly integrated silicon-based sensor chips, which are often very sensitive to mechanical stress and can therefore not be thinned using back grinding technologies.

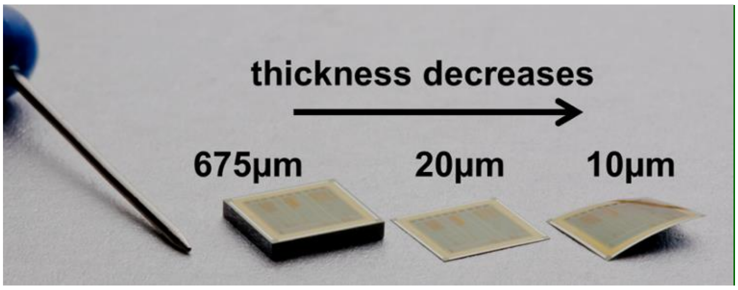


Figure 5.1 Picture of three chips with different thicknesses depicting the dramatic increase of warpage with reduced thickness. While the thick chip (675µm) is flat and the 20µm thin chip is fairly warped, the 10 µm thin chip is severely deformed

Recommendations for the further development of the wafer thinning process are an improved stress release process, better wafers handling and enhanced grinding and sawing tape materials. As the chip thickness is reduced, their deformation resulting from the built-in stress of the various IC layers increases [12], posing practical difficulties to their handling and impairing their assembly (Figure 5.1). Strategies for reducing the chip warpage, resulting in planar ultra-thin chips, can complement limitations of the wafer thinning process. A thorough understanding of the fundamental flexural limitations of the chip, both functionally and mechanically, is an important prerequisite for the integration of ultra-thin chips. Sophisticated measurement setups and test procedures need to be developed to electrically and mechanically characterize the thin chips prior and after assembly, supported by modeling and simulations so the system can already be optimized for its flexural performance during the design stage.

5.3.2 Flexible chip packaging

The availability of chip thinning processes opens interesting opportunities for advanced packaging strategies. Such a thinned chip can be embedded in a conventional circuit board, thus allowing high density integration of ICs. Secondly, the obtained flexibility of the ultrathin die opens the opportunity to fabricate a flexible package by embedding the die in a flexible interposer or PCB. Various flexible materials can be used: polyimide, PET foil, Duromer, etc. Each material requires its own fabrication technology, resulting in a flexible package with specific advantageous and drawbacks. The material/technology selection will be depending on the final device application and cost In order to cross the gap between the fine pitch technology of the chip and the coarse dimensions of the PCB technology, several competing technologies are developed with this same objective of crossing the chasm [9],[10].

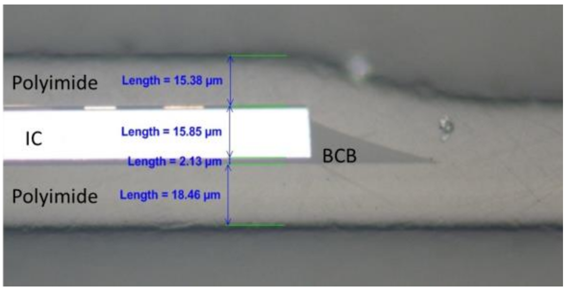
The flexibility of a system as a whole can be obtained by either making all the subparts of the system flexible or by making the rigid parts so small that they do not limit the flexibility of the system. An example of the latter is direct chip embedding in PCBs, represented below by the chip in polymer technology. While the resulting packages themselves are not flexible, the high degree of miniaturization offered by the technology enables the realization of a flexible system. Apart from the technological advantages, the strong point of this technology is the fact that it is commercially available from, for example, AT&S (ECP) or Epcos (SeSub).

The Ultra-Thin Chip Packaging technology described below combines a high degree of miniaturization with an inherently flexible chip package. The use of thin-film processing makes it possible to integrated chip with the highest complexity and a fine contact pad pitch.

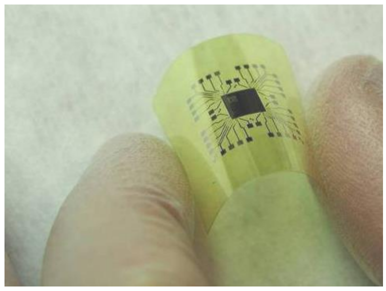
For certain applications, as for example disposable food monitoring tags, a more cost efficient packaging technology is required. By using low-cost materials and large-area processing techniques, the chip in foil approach offers a significant cost reduction over other flexible packaging technologies, while maintaining an acceptable production yield and reliability.

UTCP

The UTCP acronym stands for Ultra Thin Chip Packaging. In this patented technology a thinned chip is packaged in a polyimide membrane, on which a metal fanout pattern is deposited and patterned using thin-film techniques. In this way a flexible ultra thin polymer interposer is created, which allows the packaging of custom-off-the-shelf ICs without expensive wafer-level post-processing.



(a)



(b)

Figure 5.2 The cross-section of an ultra-thin chip package (a) illustrates the embedded IC, packaged between two polyimide layers. The result is a flexible chip package with ah metal fanout, providing the connectivity to the chip (b).

The UTCP technology differs from other approaches for thin chip embedding by its choice for combining the base material of the package (polyimide) with thin-film Cu deposition techniques for electrical interconnectivity. Fine Cu-patterns are realized with lithographic techniques.

Polyimide is interesting as a base material since it is inert to most chemicals and has a thermal budget up to 350°C, hence it does not limit the later back-end processes which are required for embedding the packaged chip in a system, such as chip embedding in a circuit board (Cfr. 5.3.3). Polyimide can be structured either by use of photolithography, either by laser ablation technology.

During UTCP fabrication, the thinned chip is attached to the polyimide film using BCB, a thermosetting polymer which is able to withstand the high temperatures needed for polyimide curing and later back-end processes.

The use of thin-film technology such as sputtering of copper and other metals allows fabrication of reliable interconnects to the chip. As the thickness of these layers can be small, a high density fanout can be realized based on photolithography. In this way the use of redistribution layers (RDL) on the IC is avoided, and the number of I/O's is not limited by the chips dimensions.

Several competing technologies with similar objectives as the ultra-thin chip package are being developed. Some of these show a strong resemblance to the UTCP technology, as for example described in refs. [9] and [10]. While the first technology is almost identical, the second approach uses a two-polymer method for encapsulating the chip. The actual encapsulation is done using BCB, but due to its brittle nature, an additional polyimide layer is needed to increase the mechanical robustness of the package. This double layer makes the processing more complex as both layers need to be crossed to realize the electrical contact to the chip.

Chip in Polymer (CiP)

Progress in the fabrication technologies for printed circuit boards opened the potential for advanced system in packages by embedding active and passive components into (multiple) build up layers of printed circuit boards. The mayor enabling technology is µ-via fabrication, using a laser ablation process to drill holes with dimensions of 30 µm in diameter and depth (the typical aspect ratio is 1). Since a PCB is essentially a compound/heterogeneous material build-up of metal layers and polymer materials, in scale production the laser ablation is typically a combination of a UV ablation for the drilling of metal layers and a far infra-red ablation (typically CO_2 laser) of polymers and glass fibers in the buildup. Electrical interconnects between layers are established by electroplating of Cu into the holes. Due to the low mechanical load (as e.g. compared to mechanical drilling) during µ-via formation in PCB, this technique has proven to be viable to connect active or passive components, which are buried in a polymer/glass fiber buildup layer of the PCB. A mayor requirement for a successful embedding and contacting is the proper contact metallization of the embedded components. Typically a 4 – 8 µm thick copper layer thickness at the location of the contact is required in order to be compatible with the laser drilling (local heat load) and to result in a low contact resistivity after the electroplating process.

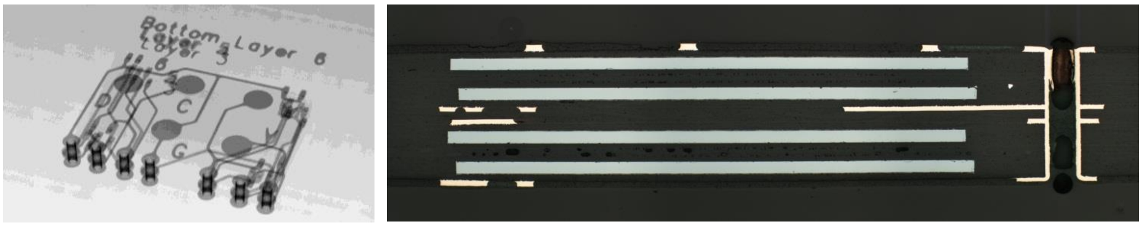


Figure 5.3 X-ray image and cross sectional view of a PCB-embedded module with 50 µm thick chips in four buildup layers. Total module thickness 420 µm.

Embedding of active and passive components has meanwhile become an industrial process for a few advanced PCB manufacturers. In order to reach desirable production robustness embedded component thicknesses are in the range of 120 µm to 150µm. Component manufacturers have responded to the trend by offering “embeddable (thin) components” with the required Cu-metallization. In spite of this, the potential of component embedding into the PCB is far from being fully exploited, the following challenges allow for interesting applications:

- The embedding technology allows for the embedding of much thinner components than currently used, such as components in a thickness range of 20 µm or less. The required Cu-thickness of the components can be reduced by using equipment with the finer tuning.
- Double sided and/or multilayer assembly of embedded components will enable an even higher integration density of electronic functionality.
- In order to enable the embedding of sensors: media (fluid, gases) access has to be provided by advanced PCB fabrication.
- Development and application of novel biocompatible or biodegradable compound materials in printed circuit boards.

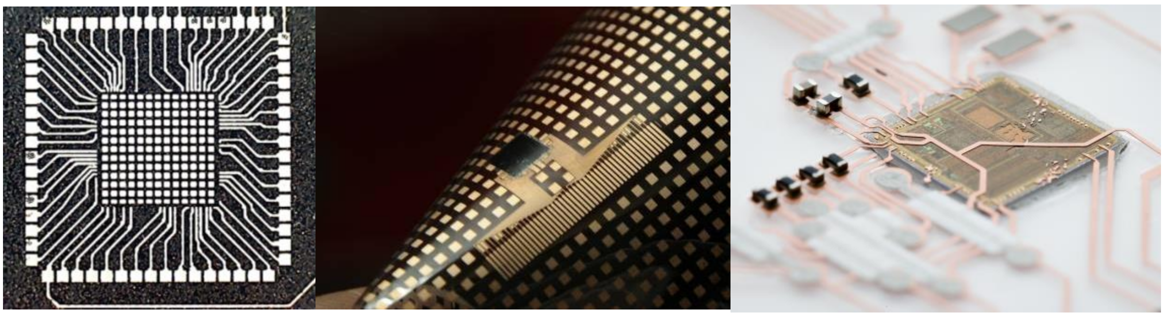
- Hermetic biocompatible encapsulation of modules (for use in implantable devices)
- Development of metallization schemes for local use of specific electrode materials such as Ag/AgCl, Au, Pt, or Pd, interesting for electrode applications for e.g. skin-contact or implantable devices

The advantage of the embedding approach for the buildup of miniaturized electronic modules is the high flexibility in design and the relatively rapid realization of products. Especially for low to medium size fabrication volumes of a specific application, the described embedding technology is economically preferable over monolithic modules.

Chip in foil

To reduce costs of smart electronic systems, cheap polyester-based substrates having (Ag) printed conductive circuitry are increasingly being used. This creates new challenges for interconnecting active and passive components. Past research into systems-in-foil focused on packaged components and surface-mount passives, resulting in a larger size and reduced flexibility. The use of ultra-thin bare dies, having thicknesses down to 20μm, allows for thin and flexible systems, but it requires pitches that are not compatible with mainstream printing technologies. Polyester films with copper metallization or using state-of-the-art printing technologies make pitches below 100μm possible at a cost comparable to that of traditional printed circuitry.

In the past few years, great advances have been made in printing technologies and printing materials. Printing resolutions down to 50 μm line and spacing can be achieved using state-of-the-art technologies like ink jet printing but also with screen and stencil printing (Figure 5.4a) [13]. The typical conductivities that can be achieved with nano-particle inks approach those of the bulk metal.



(a) (b) (c)

Figure 5.4 Overview of chip integration technologies on foil. (a)High-resolution printing of 50 μm line and spacing fan-out circuitry for bare-die microcontroller. (b) Flip-chip assembly of 20 μm thick chip with 100 μm pitch on PET-Cu foil. (c) Foil-based embedding of a microcontroller with 80 μm pitch

Low-cost plastic substrates such as PET and PEN impose temperature limitations on the assembly process, eliminating soldering as a candidate for flip-chip mounting [14]. Both isotropic and anisotropic conductive adhesives can create a reliable flip-chip interconnection within the temperature budget of the flexible polyester substrates (Figure 5.4 b). While anisotropic conductive adhesives (ACA) or films (ACF) are compatible with ultra-low pitches, the pressure required during bonding to obtain a reliable contact can be too high for the fragile ultra-thin chips [15]. Flip-chip bonding using isotropic conductive adhesive (ICA) can be achieved at lower pressure, but requires a dedicated deposition process to reach a bond pad pitch below 100 μm [16], [17]. Further development in reducing the curing temperature and time of both anisotropic and isotropic conducting as well as non-conducting adhesives is needed to increase the industrial acceptance of chip integration on flexible, low-cost substrates.

Several alternative approaches for chip integration on or in low-cost plastic foils have been developed, such as the Chip-in-flex technology from KAIST [18], Laser-Enabled Advanced Packaging (LEAP) of the North Dakota State University [19] and face-up integration using self-assembly combined with adaptive circuitry in the frame of the EU-FP7 Chip2Foil project [6]. This latter technology uses a magnetic force field to guide the chip to its final location, which seems to be a promising approach for contactless manipulation of ultra-thin chips. Recently, a foil-based chip embedding technology was jointly developed by Holst Centre and imec/CMST [20]. In contrast to fan-out WLP and chip embedding in rigid or flexible printed circuit boards, where cost reduction is achieved by scaling to larger panel sizes, low-cost was a main development goal of this foil-based chip embedding technology. The advantages of this approach in comparison to other hybrid integration methods using low-cost materials are the removal of temperature limitations for die bonding, mechanical and physical protection of the chip and the realization of a flat surface which allows for direct access to the contacts of the chip (Figure 5.4c).

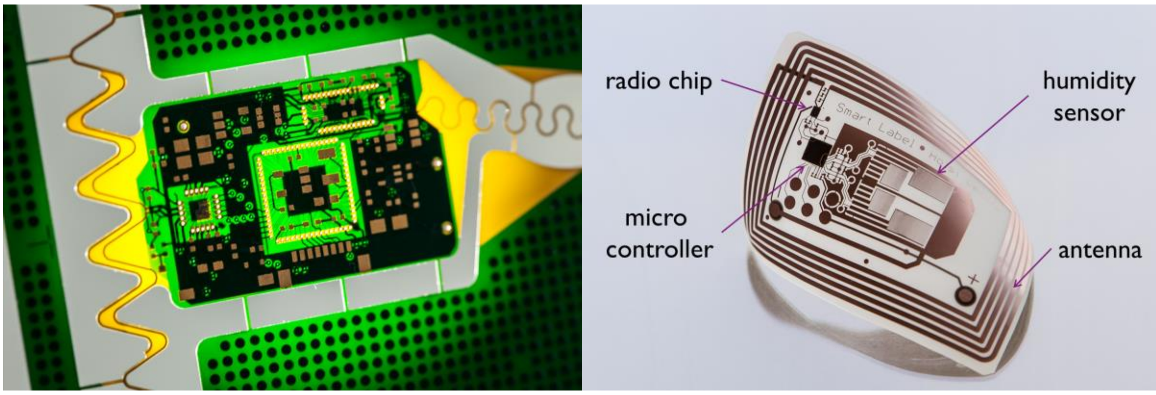
5.3.3 Flexible system packaging

Flexibility of the complete system is determined by the flexibility of the substrate onto which the components are mounted, the flexibility of the components themselves and of the interconnection between the components and the substrate. Each of these subparts can be a limiting factor in itself, but also the combination of these aspects can further limit the flexibility of the complete system. System design, component selection and choice of mounting technology can have a big impact on the mechanical performance of the system as a whole. Virtual prototyping can aid in making the correct choices during the design phase.

Flexibility of the components was partially addressed in the previous sections on chip thinning (5.3.1) and flexible chip packaging (5.3.2). Two examples of creating a flexible system based on flexible chip packaging technologies are shown in Figure 5.5: ultra-thin chip packages embedded in a flexible PCB and a complete flat, 250 μm thick, foil-based smart label, including two embedded chips, 10 embedded passives, integrated antenna and sensor circuitry, and two-layer routing.

An important oversight in most flexible packaging technologies is the integration of passive components. Compared to the ultra-thin chips, these are bulky and rigid components that have a huge impact on the size and flexibility of the total system. Passive devices integrated on a silicon die could be incorporated in the same way as bare-die chips, but these dies are often more difficult to thin down to a thickness below 50 μm without losing functionality [21]. Alternative options are the use of resistive foils and capacitor laminates [22] or thick-film polymer materials to create resistors and capacitors in situ [23]. Polyimide-based flexible packaging, such as the UTCP technology, can also be combined with vacuum deposited materials, which often require higher processing temperatures. Further development of passive component integration is vital to achieve a completely flexible System-in-Package or System-in-Foil.

The most common flexible substrate for electronic circuitry is the polyimide-based flexible printed circuit board (FCB), ranging from simple flexible cable interconnections to advanced, multilayer substrates. PCB manufacturers are continuously improving their processes and expanding their capabilities with respect to layer thickness (down to 12.5 μm), copper thickness (5 μm and lower), feature size (25 μm L/S) and via size (25 μm diameter).



(a) (b)

Figure 5.5 (a) Three UTCPs (microcontroller, radio chip and analog frontend) embedded in a four-layer flexible PCBsmart label, including two embedded chips, 10 embedded passives, integrated antenna and sensor circuitry, and two-layer routing

Endicott Interconnect recently demonstrated a 12-layer board with a total thickness of less than 200 µm, which could be bend with less than 3 mm. (b) Complete flat, 250 µm thick, flexible radius [24]. Companies as Dyconex, Cicor Microelectronics and HighTec are taking one step further by using thin-film metallization and spin-coated dielectric layers to achieve higher flexibility. These substrates can be folded around the components to fit inside small housing such as for example swallowable capsules [25]. Extreme flexibility that allows the substrate to be crumbled like paper can still only be achieved with organic electronics [26].

Cost reduction in medical applications and other flexible systems can be achieved by combining a low-cost, foil-based substrate with high-density patches that allow the integration of more complex functionality. Data processing and wireless communication require integrated circuits with higher I/O count (> 40 I/Os) and small pitch (< 100 µm). By limiting the high-density (HD) circuitry to dedicated patches, the remainder of the system can be realized using low-cost foil-based circuit and integration technologies. The ultimate cost saving can be achieved by re-using the HD patch and making only the foil part disposable.

5.4 3D chip stacking

5.4.1 3D Chip stacking using Through-Si-Via (TSV) technology

Application drivers

The development of 3D-TSV technology is driven by applications such a high density memory stacking (Memory stacks), wide-I/O memory direct access to logic devices (Memory on logic stacks) and other heterogeneous stacking applications such as analog-digital stacks [27]. For high performance applications, the heat removal from a 3D stack may limit its usefulness. Also in other cases, system integration may require a variety of components that are not available for 3D-TSV integration. In that case, a so-called “interposer” or 2.5D stacking approach is used, as illustrated in figure 5.7. For such approach, the TSV is integrated in a separate substrate (“the interposer”) and die, or die-stacks, are attached to the interposer front side.

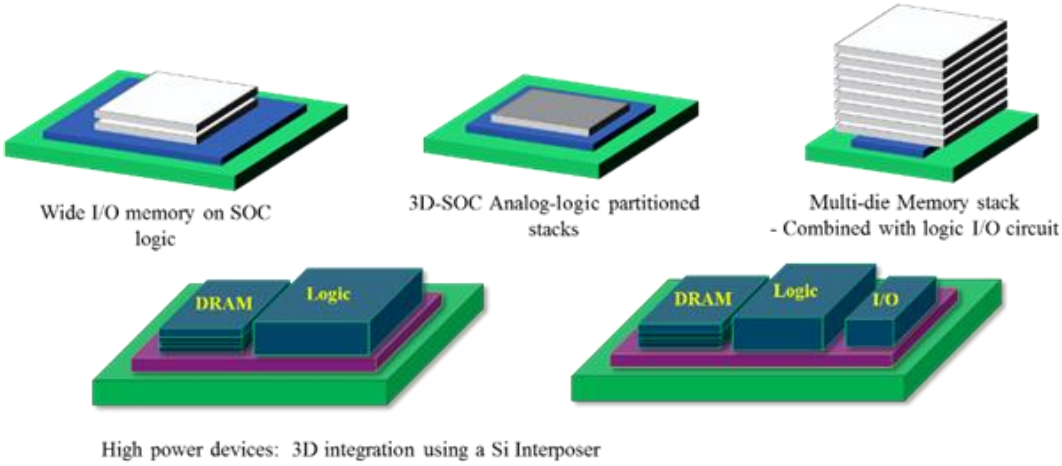


Figure 5.7: Applications driving the technology for 3D-TSV integration

The 3D-TSV integration process flow

A large variety of TSV integration schemes have been proposed and studied. However, most integration schemes use one of only two main integration schemes: via-last, TSVs are formed after completing the IC fabrication process, and via-middle, TSVs are formed during the IC process flow, in particular after the front-end transistor flow, but before the BEOL interconnect flow. Today, the dominant approaches for TSV use Cu as TSV conductor material.

Via-Middle TSV processing is the predominant approach used today for high density TSV integration in CMOS wafers and Si-interposers, TA typical implementation is shown in figure 5.8. After front-end processing and just prior to the first Cu-damascene metal layer processing, the TSV via hole is etched in the Si wafer. The deep RIE-etching of the TSV hole is followed by the conformal deposition of an insulating dielectric layer.

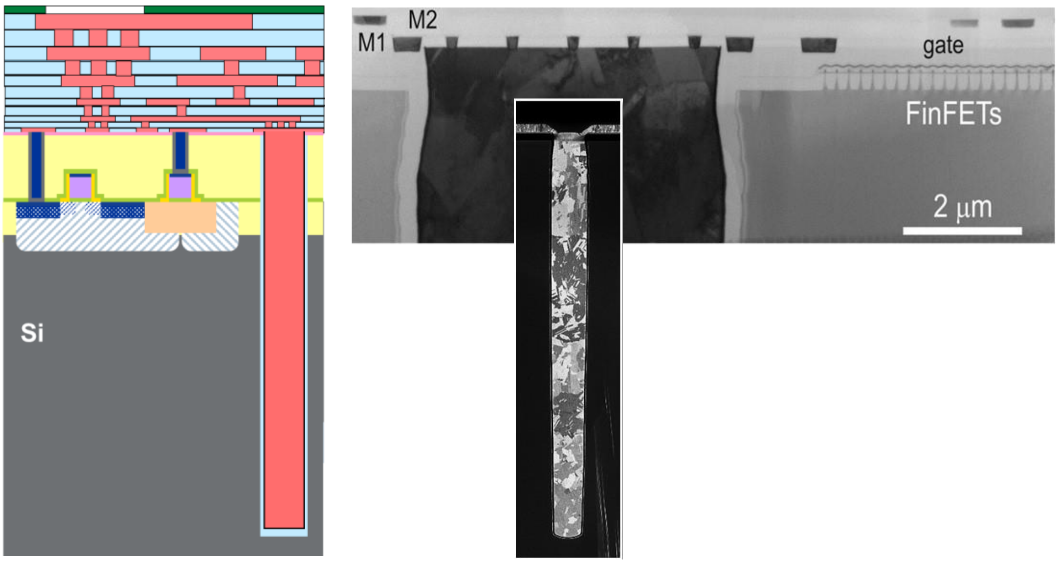


Figure 5.8: Left: Via Middle integration between Front end and back-end process. Right: Example via-middle integration in FinFET CMOS device wafer (source imec). TSV diameter is 5 µm, depth is 50µm

Next, the TSV metallization is performed. First a Cu diffusion barrier and a thin Cu seed layer are deposited by physical vapor deposition, PVD, of respectively Ta and Cu. This is followed by the bottom-up Cu-via fill by electro-plating. The Cu is annealed after this step to avoid the so-called "Cu-pumping effect" later in the process flow [28]. The TSV process is finished after a CMP step of the Cu overburden, the Ta seed and oxide liner from the field area of the wafer. Our current process of reference is a 5 µm diameter, 50 µm deep TSV, as illustrated in figure 5.8 [29].

After TSV processing, the regular processing of the back-end of line layers is continued on the device wafers. After finishing the wafers, they are ready for wafer thinning and exposure of the TSV's at the backside of the wafer [30]. This requires bonding of the wafers to a temporary carrier prior to high precision wafer thinning [31]. The most popular approaches use Si wafers or special glass wafers (Si-CTE matched) as carriers. Currently the dominant temporary glue materials are those that allow for room-temperature, "peel"-debonding of the thin wafer or those that use laser-debonding (only for glass carriers).

Using such approaches, a defect-free wafer bonding can be obtained with a total thickness variation of the thinned wafer of less than 2 µm, as illustrated in figure 5.9 [31]. Such thickness control is required in order to use a so-called soft-via reveal process: the Si is ground back, not exposing any of the TSV. This is followed by a dry or wet recess etch of the Si backside surface of the wafer, exposing all TSV at approximately the same time, but without removing the oxide liner still covering the TSVs. After this process a backside passivation layer is deposited. A self-aligned recess etch is then used to expose the Cu of the TSVs at the backside of the wafer, as shown in figure 5.9. Alternatively a backside CMP process can be used to expose the Cu TSVs after backside passivation. Next, a thin film backside redistribution layer (RDL) and µbumps can be processed using wafer-level packaging techniques. Finally the thin wafers can be debonded from the temporary Si carrier and diced. They are then ready for 3D stacking.

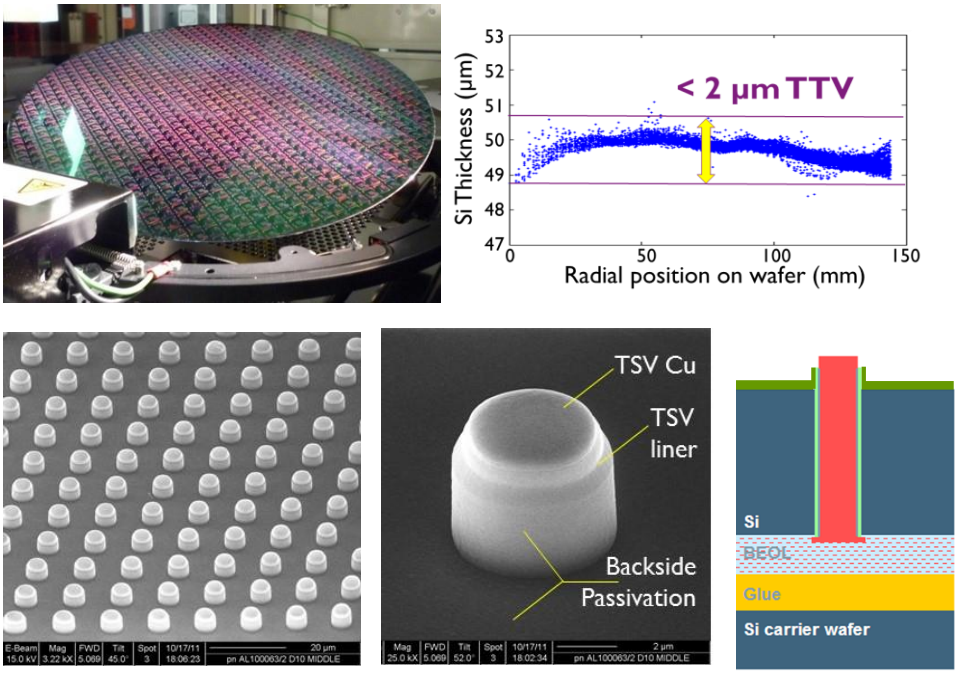


Figure 5.9: Backside "soft"-Via Reveal of a 300mm diameter CMOS wafer, thinned down to 50 µm with a total thickness variation (TTV) below 2µm. (source imec)

5.4.2 PoP as alternative for TSV based 3D stacking

UTCP Stacking

An alternative approach towards extreme miniaturization of systems with multiple ICs in a package is to reduce the area which is occupied. This can be done by stacking multiple UTCP-packaged dies on top of each other using lamination technology, combined with the fabrication of the interconnections between the layers using via-drilling and via-filling by electroplating of the metallization. Such a stacked UTCP is not flexible anymore, but an extreme degree of miniaturization is realized: in a package of about 300 µm thick, 4 dies can be embedded and interconnected [32]. The final result is shown in Figure 5.10: a carrier substrate with multiple flat UTCPs, and the finally obtained stacked EEPROM system, consisting of 4 stacked UTCPs and being an example of extreme miniaturization.

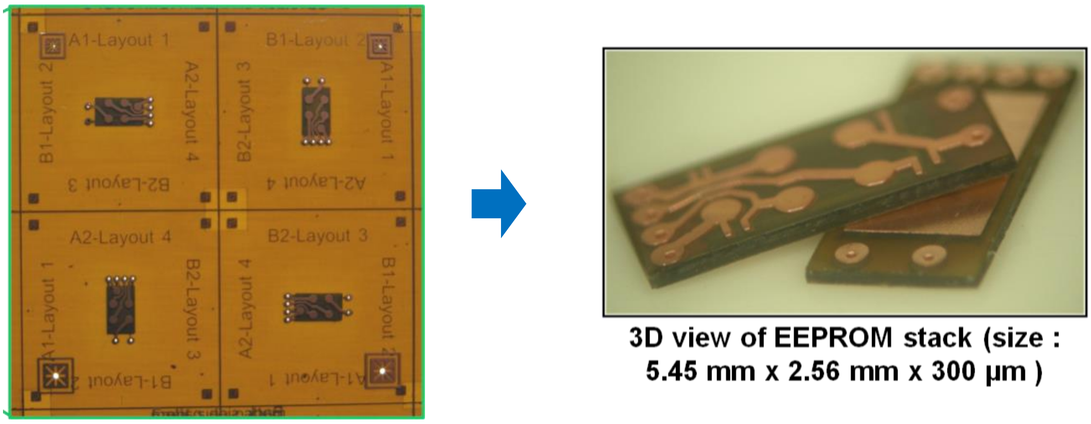


Figure 5.10 (left) a UTCP carrier substrate with 4 UTCPs, ready for stacking;
(right) the EEPROM memory device consisting of 4 stacked dies, all in a package of only 300 µm thick

5.5 Stretchable interconnects/electronic circuits including textile integration

5.5.1 PCB (printed circuit board) based stretchable circuits

The fabrication of stretchable electronics systems has evolved during the past decade from an academic curiosity into technologies compatible with the industrial value chain, comprising the fabrication of a stretchable printed circuits board, assembly of electronic components and encapsulation of the stretchable matrix. Two different mainstream approaches have been developed up to a considerable maturity level: one is based on the molding of the electronic circuitry into a stretchable matrix (PDMS or polyurethane), the second one on lamination of thermoplastic polyurethane foils similar to the conventional build-up of a multilayer printed circuit board [33-35].

Typical thicknesses of stretchable electronics realized with these technologies are in the range of 150 µm to 2 mm (generally systems made with PDMS are thicker). For both technologies the basic approach to realize stretchable interconnects is a meandering layout of copper lines (instead of straight lines as in conventions printed circuit boards). Component assembly to a stretchable substrate follows the conventional SMD (surface mount devices) approach, with lead free (soldering temperature 260 °C) or a commercial low temperature solder (SnBi, soldering temperature 160 °C). The latter is preferred for thermoplastic stretchable matrix material with softening temperatures of 170-180°C. After component assembly the whole electronic system is typically embedded in the stretchable matrix, leaving only accessible electrical contacts for external power supply and/or data transmission.

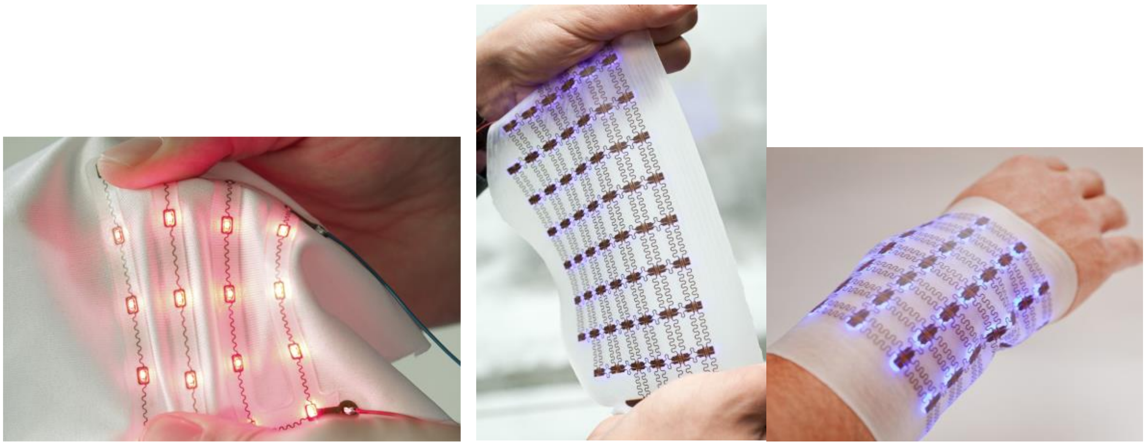


Figure 5.11: (left) stretchable LED matrix including SMD LEDs and stretchable interconnects embedded in TPU and applied to a textile – (right) Stretchable light therapy device for RSI treatment including blue SMD LEDs and stretchable interconnects encapsulated in PDMS

There is still large potential for further developments in stretchable electronics fabrication. One of the basic topics is dedicated development of stretchable matrix materials. As a matter of fact the materials used currently are not developed specifically for use in stretchable electronics. Improvements with respect to moisture uptake, break through voltage, and dielectric constants would allow for better performance of the fabricated systems. Promising targets for future matrix material improvements are application certified biocompatibility, softness grades, color and material thickness. Other technological targets for future developments are thinner stretchable systems which can result into even smaller devices standing systems., or more complex system build ups with graded material characteristics, such as stiffness, refraction index, etc., which will significantly improve adaptability of the interface between the electronics and the human skin without losing device robustness. For certain biomedical devices, conductor structures, which are to date consisting of Cu, will have to be replaced by alternative biocompatible conductors or at least encapsulated by an appropriate surface finish, e.g. Au or Pt. Finally, stretchable technology would also take profit of the developments ongoing for improvement of integration of components into rigid PCBs. The smaller/flatter components can be integrated in stretchable substrates too, resulting in highly compact stretchable devices.

In order to broaden the range of applications, implementation of sensors and actuators into the stretchable devices has to be addressed. With this respect methodologies to provide media access (to liquids or gases) to sensors (commercial SMD types) embedded into the stretchable electronics have to be developed. For certain applications, the realization of sensing and actuating structures just using the stretchablity and physical properties of the matrix materials themselves would be an interesting scenario.

5.5.2 Thin-film based stretchable circuits, incl. thin chip integration

Next to PCB inspired stretchable circuits, using typically 17µm or 35µm thick Cu metallic interconnections, also thin-film technology based stretchable circuits are being developed. These make use of PVD (physical vapor deposition, e.g. sputter deposited) interconnections, patterned by lithography and wet etching or lift-off techniques. The thickness of the thin-film interconnection usually is below 1µm, making line widths down to

20μm possible (typical for thin-film technology), so higher interconnection densities can be obtained, compared to the PCB based stretchable circuits of par. 8.5.1.

In one approach the thin-film interconnections are deposited onto a perforated (flexible) polyimide carrier, allowing deformation and stretching in certain directions [36]. In a second approach ultrathin metals are deposited on elastic polymers like PDMS (poly-dimethyl siloxane, widely known as "silicone"). The metals are patterned as straight lines, and functionality under elongation is guaranteed by intrinsic stretchability of the ultrathin metal [37].

The most successful and promising approach, adopted both by research institutes and emerging industry, is the one whereby thin-film interconnects are patterned into meander shapes. The interconnects are supported by a spin-on polyimide, also patterned as a meander, and the meander structures are embedded in an elastic polymer like PDMS [38]–[41]. Functional circuits, using this technology have been produced, by integrating batteries, LEDs, sensors and transistors with the stretchable interconnections [40],[41]. As an example figure 5.12 shows the integration of an UTCP packaged microcontroller (mentioned in par. 5.3.2), with a thin-film stretchable circuit. Adding SMD passives and LEDs resulted in functional demonstrator circuits [42]. In figure 5.13 the so-called 'electronic skin' is shown, an ultra-thin sensor system with mender shaped interconnects, which sticks to the skin without adhesives and which is able to follow the local skin movements.

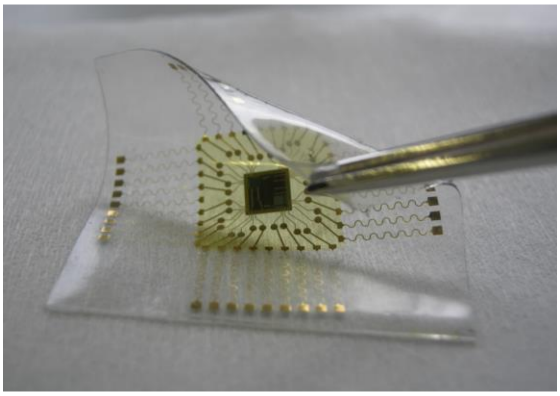


Figure 5.12: Bendability of UTCP (ultrathin chip packaged) TI-MSP430F1611 Microcontroller in thin-film stretch circuit. Meander shaped interconnects are clearly visible.

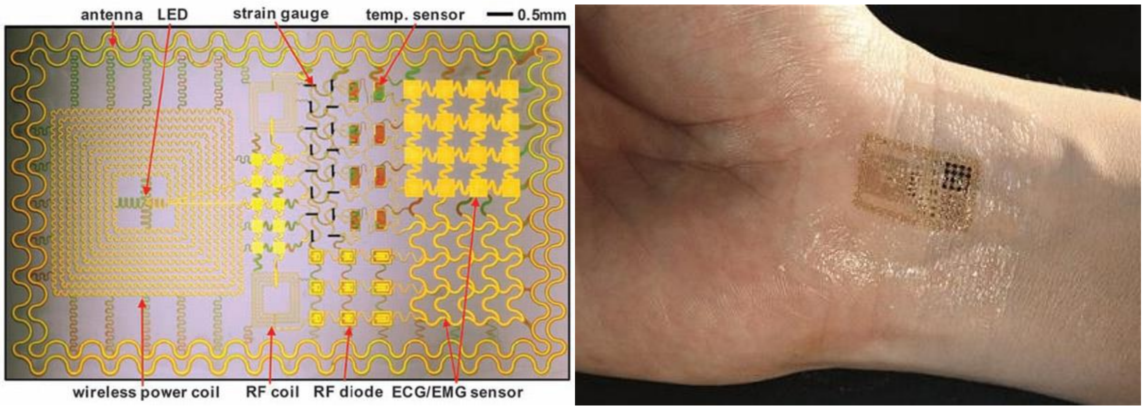


Fig. 5.13: the so-called 'electronic skin' technology developed by Rogers and co-workers [6], left a schematic system view, right a photograph taken after application to the skin. Electronic sensors are embedded in a film thinner than the diameter of a human hair, which was placed on a polyester backing like those used for the temporary tattoos popular with children. After application onto the skin, the sensor is flexible enough to move with the skin and it adheres without adhesives.

5.5.3 Thermoformed electronic circuits

Thermoforming of electronic circuits and systems is a relatively new field of development, triggered by requests from product designers for more freedom in the shape of diverse appliances, while keeping manufacturing cost within reasonable limitations. A promising approach to respond to these requirements is the planar fabrication of electronics in as much a conventional manner as possible -fabrication of a circuit board, assembly of components, encapsulation- and subsequently to deform the electronics putting them into the shape conceived by the product designer. Hence the device will be stretched and bend only one single time. First developments in this direction are under way. Targeted carrier materials for the deformable electronics are thermoplastic materials such as polycarbonate and polyurethane, but also materials which can be draped respectively and fixed into a desired shape, like PDMS. Research and development targets of the ongoing initiatives are design guidelines for the electronic systems to be deformed, process technologies and their constraints, as well as the setting up of potential value chains.

Research topics beyond the ongoing programs should focus on materials and respective process developments, where electrical and mechanical characteristics of the thermoplastic substrates can be improved (potentially with specific application cases in mind). Thereby the complexity of materials and their combinations as well as the respective processing technologies will increase and need further adaptation for the industrial fabrication schemes. Implementation of generic sensor structures within the deformed electronics will also be a promising field of investigation (for low cost sensing/actuating systems): shape memory functionalities, electrical or mechanical feedback structures will provide pathways to further potential applications.

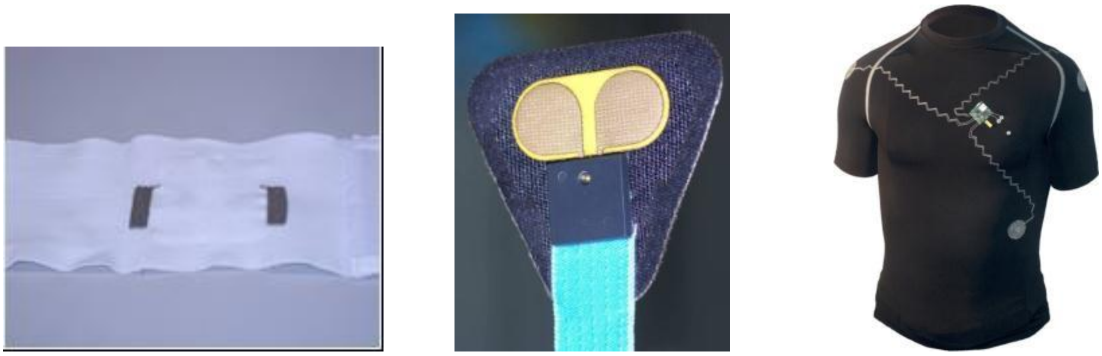
5.5.4 Integration of electronics into textiles

Smart textiles are fabrics with integrated additional functionalities based on microelectronics and microsystem technologies. Already from the beginning the term was used to describe fabric with integrated and interconnected sensors. Smart textiles benefit from being flexible and stretchable and is therefore for suitable for close to the body use e.g. for measurement of physiological parameters.

There are 3 different levels of integration in smart textiles:

- Add-on: Conventional electronic components and conductors are mounted onto the textile substrate. An example is shown in Fig. 5.13.b. Miniaturisation of modules is desired to maintain the textile properties, but especially stretchability is compromised by the wiring.
- Partial integration: some components are integrated into the textile substrates. In a first step the conductors are integrated during the fabrication of the textile or applied to substrate afterwards (e.g. embroidery, printing) using textile yarns or conductive inks/pastes. An example is shown in Fig. 5.13.c.

Seamless integration: All components are fabricated using textile technologies (fabrication of the substrate carrier, conductors, sensors, coating, finishing, etc.), e.g. the woven sensor in Fig. 5.13.a. Examples of seamless integration include stretch sensors based on conductive yarns or optical fibres, capacitive pressure sensors, both based on a multilayer structure, where the outer electrodes of the capacitor are either made from conductive yarn or a conductive coating a dry skin-contact electrode for measuring an ECG signal [45][33].



a) b) c)

Figure 5.13: a) woven stretch sensor, b) laminated EMG sensor, c) embroidered ECG electrodes

An important and critical step in the development of a manufacturable and reliable smart textile system is the mechanical and electrical connection between electronics and textiles. The most commonly adopted approach is based on textile conductors with or without insulation and adhesive bonding (isotropic conductive adhesive) or soldering with a low melting temperature type solders. Insulated conductors always have the difficulty of an additional step to open in the insulation, e.g. by thermal or laser ablation. This can be overcome by mechanical force-fit interconnection methods like crimping [44]. Another approach is the contacting by embroidery, for which commercially available modules already exist (e.g. LilyPad). This technology does not allow miniaturization of the electronics, it works only with non-insulated conductors and in harsh environmental conditions reliability problems have been observed, hence this technology is used mainly for prototypes.

Various research institutes as well as companies (e.g. Philips, interactive wear, adidas) developed smart textiles for different applications. As the focus is usually more on the realization of the application, and less on the technology optimization, there is still a necessity for qualified processes.

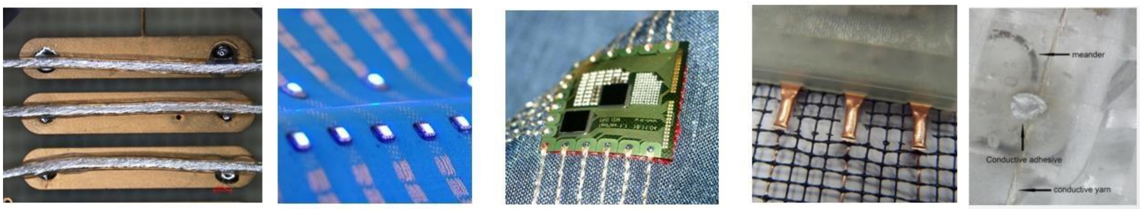


Figure 5.14: Textile conductors from left to right: Soldering, NC-Adhesives, Embroidery, Crimping, Conductive adhesives

There is a growing need for seamless textile integration of sensors together with an optimized integration of the data processing units and wireless interfaces. Sensors and electronics should still allow stretchability of the final textile and hence give comfort close the body. The majority of conductors, interposers and encapsulation materials currently used are not biocompatible or they are not yet tested for biocompatibility. New materials and material combinations have to be developed and qualified to achieve this. Furthermore, for applications where washability is a requirement, the technologies should be adapted (design, materials, etc.) in order that they can withstand the mechanical impact as well as the effect of the waterand cleaning chemicals.

The overall lack of standardized processes and equipment as well as qualification procedures for smart textiles is a major reason for the lack of products on the market.

5.6 Packaging and integration aspects for implantable devices

For implantable electronic devices, very special device packaging is required, due to the particular environment the device will be placed in. During device operation, it will function in a chemically aggressive wet environment. The specific chemistry of the local tissue depends on the implant site. Opposite to this, the implant resides in a very easy environment regarding exposure to thermal variation and vibrations. Immediately after fabrication, the device needs sterilization, hence the system has to be developed such that common sterilization techniques can be applied without any device damage. In case the device is used many times after short contact with human tissue, exposure to many sterilization cycles should be feasible. Due to the very special requirements for packaging an implantable system, dedicated packaging technologies are developed. Recently, due to the myriad of possible implantable devices currently under investigation, a whole variety of packaging solutions is heavily researched, each to solve the specific needs of the implant. Only a limited amount of standards exist to test the quality of implantable electronic devices, hence still a lot of testing is performed by using test protocols developed for automotive or space applications. Furthermore, accelerated testing, typically performed by testing under elevated temperature conditions, is often impossible or useless for implants, since the used materials might degrade at higher temperature, while it will serve its function perfectly at 37°C. The need for more dedicated standard tests for electronic implants is clearly existing; some research groups spend efforts to address this gap but much more research is needed [43]. Finally, before a medical implant can be brought to the market, FDA approval/CE labeling etc. is essential. This procedure is difficult, costly and time-consuming, and lack of experience in this approval procedure might result in the situation that interesting feasibility studies or prototypes never make it into a full product available on the medical market.

5.6.1 Introduction: bio-response of the human body upon implantation of foreign material

Before discussing packaging approaches for implanted medical devices, two major (problematic) issues are explained related to device implantation: (1) the foreign body reaction (FBR) which is the natural reaction from tissue upon an implanted foreign material, and (2) infection/biofilm formation, a risky complication which might occur after device implantation.

The ***Foreign Body Reaction*** (FBR) is the natural reaction from a body on the implantation of foreign material, starting from acute inflammation of local tissue and accumulation of monocytes/macrophages at the wound site. These white blood cells clean the wound area from debris and bacteria's, but they try also to digest the implanted material, first as individual cells, later by fusing together to form so-called *foreign body giant cells*. Finally, after unsuccessful attempts of these foreign body giant cells to digest the implant, a dense layer of connective tissue is formed, walling off the implanted material/device from the body. This connective tissue will ensure mechanical anchoring of the implant, which might be advantageous. But for most implanted sensors, this walling off by connective tissue results in unreliable sensor measurements since the sensor surface is not in direct contact anymore with the soft tissue. Various factors modulate this FBR: the chemistry of the surface of the implant, the morphology, the porosity of the surface material, the mechanical properties,.. all have an influence on the FBR. Currently, a lot of researchers investigate these complex relations in order to reduce the FBR. In general, one can state that the more the implant material resembles the local tissue, hence the more biomimetic the material is, the milder the FBR.

Infection upon implantation is a definitive risk associated with implants, causing a lot of problems and costs related to extra medication, longer hospitalization, and in a considerable amount of cases total removal of the implant. In spite of implant sterilization and stringent rules regarding prevention of infections in the operation room, bacteria might enter the body during implantation. White blood cells present in the implant area will try to clean up all debris and bacteria, but when sufficient bacteria are present, they might attach to the implant surface and form so called *biofilms*: bacterial colonies covering the implant surface. Such colonies are very difficult to destroy by antibiotics, hence prevention is of utmost importance. Various properties of the surface of the implant will strongly influence the risk of biofilm formation. As a general rule, one can state that an implant is less sensitive for biofilm attachment in case the local tissue cells have a strong affinity to attach and populate the implant surface. Surface roughness, used material and coatings, presence of antimicrobial drugs or cell growth factors, etc. will influence the affinity of healthy cells versus bacteria to attach and proliferate on the implant.

5.6.2 Requirements for the package of an electronic implant

Listed here are the most important package properties which are essential for all implanted devices. Since a huge variation of possible electronic implants is currently researched, a variety of additional packaging requirements will exist for each specific application.

- *Biocompatibility:* Careful selection of materials and package fabrication processes is needed to ensure a device embedding that is biocompatible. Biocompatibility has been defined as "the ability of a material to perform with an appropriate host response in a specific application" [47]. An appropriate host reaction includes no local tissue damage due to cytotoxicity, limited FBR and no short or long term adverse body effects. Remark that this definition points out that there isn't an absolute status of biocompatibility: it is a contextual concept; site and duration of the implant, as well as type of material-body contact are important parameters. The ISO 10993 standard is internationally used as a reference for all testing related to biocompatibility and biostability of materials and implantable devices.

- *Biostability*: The device package should withstand his harsh bio-environment for the total implantation period. Materials should not degrade, or their degradation should not cause harm to the implanted electronics, while the degradation products shall not harm the host tissue.
- *Hermeticity* of the package: The device package should form a bi-directional diffusion barrier: no biofluids should penetrate into the electronic device risking corrosion or other damaging effects, and no harmful components in the electronic device (such as Copper) should diffuse through the package into the host tissue, being responsible for adverse effects on the human body.
- *Suitability of package* (and total device) with common sterilization procedures
- *Suitability of package* with the selected data/energy transfer method (RF based (typically 400MHz), magnetic induction, acoustic transmission, etc.)
- *Required mechanical properties* to protect the electronics (and the body) during device operation, for the total lifetime of the implant. Examples: required flexibility for moving parts, required resilience to avoid package cracking upon impact,...
- *Desired possibilities*: MRI compatible electronic device, miniaturized package to allow for minimum invasive implantation, and cost effective package.

5.6.3 Traditional electronic implant package: a Titanium enclosure for the electronics combined with polymer encapsulation for leads and electrodes

Traditionally the electronic part of an implantable device such as a pacemaker or a cochlear implant is packaged in a rigid Titanium (Ti) box to ensure hermetic and biocompatible packaging of the microelectronics. The use of such a Ti-box has clear advantages: Ti is a material with good and well-known biocompatibility, simplifying the approval process for bringing an implant to the market, and dedicated welding processes ensure an hermetic enclosure of the electronics. On the other hand, as a consequence of the high temperature welding process to make the Ti-box hermetic, this box is often large compared to the electronics inside to avoid damage during welding, hence a larger insertion wound is needed for implantation, with a higher infection risk upon implantation as a consequence. The size of the Ti-package combined with the rigidity of the box is in strong contrast with the soft tissue surrounding the implant, hence a pronounced Foreign Body Reaction (FBR) and adverse effects such as irritation upon muscle motion are more likely (See [48][49]). Transmission of RF signals through the Ti box is not ideal, a considerable loss of power will result. Magnetic transmission is impossible through a Ti-box. For this type of transmission, the transmittance coil will be packaged in a silicone embedding connected with the Ti-box containing the electronics.

Figure 5.15: The implantable portion of the cochlear implant: (1)Transmitter coil in a silicone sheath; (2): Electronics enclosed in a titanium casing; (3): Electrode with platinum contacts in a silicone array; (4): Cochleostomy site; (5): Silicone cable in the middle-ear/mastoid region. (Photograph from Stöver at al, see [50])

The leads of a pacemaker, or the wires and electrode area of a cochlear implant, are traditionally fabricated from biocompatible conductors (typically platinum, Platinum/Iridium) covered with biocompatible insulation material (such as Teflon, Parylene-C), finally embedded in a medical grade PDMS or polyurethane encapsulation. The soft polymers provide the essential flexibility and mechanical stability for the leads/ electrode area. Risks of cracks in the embedding polymers or insulating material due to long time exposure to tissue movement are existing, hence there is still room for material improvement. Hermeticity by silicone embedding is limited, hence the selection of corrosion resistant conductors is essential for medium to long term implantation. The development of fibrous connective tissue is typically pronounced when using silicone embedding, which is disadvantageous at the location of electrodes, since a higher electrode-tissue impedance will result, causing a larger power consumption of the device and/or less sensitive biopotential sensing. Currently, dedicated drugs are applied at the electrode site during the first weeks upon implantation, in order to reduce this growth of fibrous tissue. Most often these drugs are administered locally by a drug releasing or biodegrading drug-containing coating. The use of a more biomimetic polymer encapsulation is an alternative method to avoid excessive connective tissue growth. This approach is heavily researched at this moment, but more investigation is still needed to use this method as tissue growth inhibitor in commercial available implants.

Conductors in electronic devices for long term implantation are often from gold or platinum, combined with Iridium for better mechanical properties. Gold and platinum are showing excellent biocompatibility and corrosion resistance, but these materials are highly expensive. Often these metals are deposited using lift-off or other subtracting fabrication methods, making the total process even more expensive since an important part of the deposited metal is never used. Research towards cost effective additive techniques such as selective electroplating of gold or platinum is ongoing [51].

5.6.4 Advanced packaging techniques for electronic implants

By using alternatives for the Ti-box, miniaturization trends in packaging of microelectronics will be extended towards packaging of implanted electronic devices, which might result in the use of minimum invasive implantation techniques, with reduced FBR and less risk on biofilm formation. Moreover, by selecting the proper materials and/or surface treatments/coatings, the final package can be made soft and biomimetic, reducing even more the risk on pronounced FBR and adverse effects.

Various advanced packaging concepts are currently under investigation, a summary is given below.

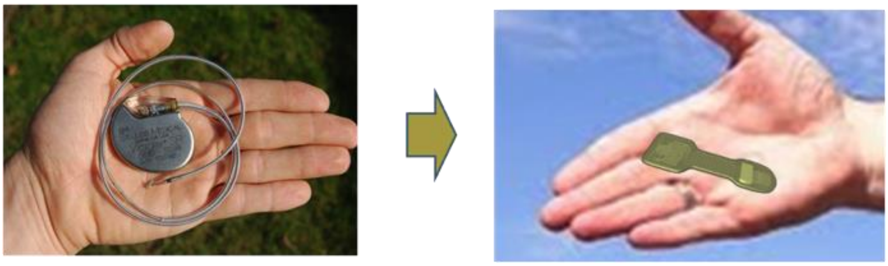


Figure 5.16: the traditional Ti-box type package can be replaced by an advanced implant package: a biomimetic skin-type packaging will result in a comfortable implantable device, causing limited FBR and other adverse effects.

Ceramic packages/ sealing layers

Ceramic packages have been used in the past and showed a higher risk on breakage upon impact and a worse hermeticity then a Ti enclosure, hence ceramic packages have not been popular. Nevertheless, ceramic materials have interesting properties such as a better transmission of RF signals. Currently, researchers at Valtronic are developing dedicated fabrication techniques of glass embedding, which result in better hermeticity and less RF signal loss, combined with a package miniaturization allowing for minimum invasive implantation techniques [52].

Other researchers use (a stack of) ceramic layers in order to stop diffusion and create an hermetic sealing of an electronic chip. At imec, a wafer level based sealing procedure for chips is developed, using standard ceramic clean room materials which are biocompatible such as Si-oxide, -nitride, -carbide [53]. Metal bondpads on the chips are sealed using layers of biocompatible conductors as Ti/TiN and platinum.

Although very interesting results show clear potential of ceramic packages or layers, more experiments are needed before using this approach in commercial implants.

Use of polymer based packages

Various biocompatible polymers are heavily studied in order to use them as packaging encapsulation to replace the Ti-box. Since a variety of properties have to be realized, for most applications a polymer based encapsulation will be combined with other functional layers such as diffusion barriers. Interesting encapsulation materials are advanced biocompatible types of polyurethanes, silicones, teflon, polyimides,... These materials are still optimized by polymer manufacturers, in order to improve mechanical properties, adhesion to underlying materials or subsequent device coatings, to avoid swelling by water uptake upon implantation, etc.

In case a bio-chemical sensing area is present on the implant, the encapsulation material should not cover this bio-chemical sensor, hence etch or laser ablation techniques have to be developed to realize functional windows in the encapsulant, without leaving traces of poisonous etchants or debris of ablation. Development of photopatternable encapsulants is an interesting future option too. Research is still needed, since up to now photopatternable polymer materials are not biocompatible.

All these encapsulation polymers are in direct contact with the local tissue, hence the material-tissue interaction is very important, and surface modification techniques or the application of dedicated functional coatings might be essential to ensure the optimum biological response (see further for more details).

Various research groups are working at advanced implant packaging solutions. As an example, an implantable packaging approach currently under development at imec is shown and summarized in Fig. 5.17 , see also [53-54].

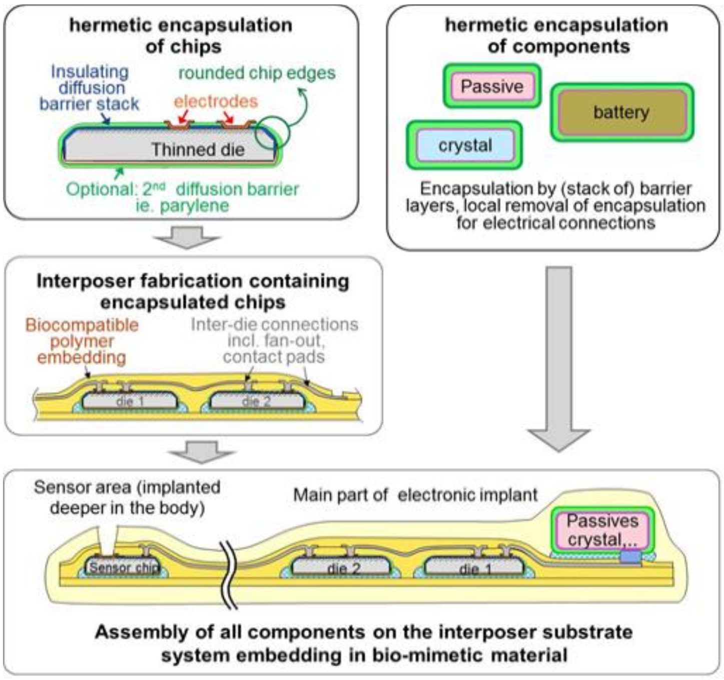


Figure 5.17: overview of implantable package process (Source imec)

Since the reliability of the package should be very high, the package consists of various levels. First each chip or subcomponent is packaged individually in a hermetic encapsulation made by bi-directional diffusion barrier such as parylene-C or stacks of organic/inorganic layers. In a next phase, all chips are encapsulated in a so-called interposer, using an implantable polyimide as carrier. Finally, all sub-components are assembled on a carrier and packaged using a biocompatible system encapsulation, such as an implantable PDMS or polyurethane. Metal interconnects are typically from gold or platinum due to their excellent corrosion resistance. Obviously all materials used for this packaging technology are biocompatible and both components and package materials should be suited for sterilization. Since biocompatibility is dependent on the duration and location of the implant, material selection might be optimized towards a specific application.

Modification of the implant surface

In order to reduce the biological response (hence FBR, biofilm growth,..), the implant surface can be modified to enhance cell adhesion and/or proliferation, to promote hydrophobicity, to reduce bacterial growth, etc. Since the optimization of the biorespons upon implantation is of utmost importance, various modification techniques get a lot of attention in the research community:

- *Physical functionalization*: by altering the topography/roughness of the surface, or by creating a well-controlled microstructure, the interaction of cells with the foreign material might by strongly influenced. Even if structures differ only a few nanometres in size, they can result in very different cell-material interactions [50].

- *Biochemical functionalization:* binding chemicals to the implant surface which function as signalling products for the host tissue, offers interesting possibilities to change the cell-material interaction. By binding proteins to the implant surface (also called grafting), certain bio-responses are promoted. Growth factors are popular proteins for this application, enhancing local tissue cell proliferation.
- *Biological functionalization:* Also functionalization performed by adhering stem cells to the surface is investigated [50].

Use of dedicated functional films/coatings

In order to create a reliable *bi-direction diffusion barrier* surrounding the electronic implant, thin films of dedicated materials might be applied, such as Parylene-C, Parylene-HT, Parylene layers combined with very thin layers of ceramic materials, Alucones etc. [54]. Parylene is a popular hydrophobic polymer family used in the past already to protect conventional PCBs from corrosion. Several Parylene types are biocompatible and find already a wide application for short term implants (corrosion prevention of short term implants, or lubrication of passive devices such as catheters). For long term implants (> 10 years), conventional parylene films are not sufficient for corrosion prevention. Material improvements or the combination of parylene with other films such as thin ceramic coatings, or the development of new barrier materials such as Alucones might be essential and is currently attracting attention from the research community. The lack of good accelerated test protocols for this kind of issues is a clear problem, and forces research groups to investigate also test methods as well as the performance of new materials/ new combinations of barrier films.

- *Drug delivering coatings* are interesting study objects, offering a possible answer to a variety of problems related with the FBR or infection/biofilm prevention. Such drug containing coatings are applied on the outside of an implant, and drugs are released at the implant site by well-known diffusion effects or degradation of the coating. Drugs will be released for a limited period of time, typically 1-2 months. Various drugs show interesting possibilities: antibiotics to fight infections (see further), growth factors to improve cell proliferation of local tissue, drugs decreasing the growth of fibrous tissue as a result of the FBR, etc. Early stage investigations in this area are typically performed by medical/pharmaceutical specialists, while it is essential to realize a strong collaboration between these scientists and engineers developing the implantable device, in order to converge towards a functional and manufacturable solution.
- *Antibacterial coatings* are gaining research attention, since the medical world observed clearly that an important amount of complication of implants deals with infections at the implant site (biofilm formation). Such infections can occur during the first 1-2 months after implantation, related to the surgical procedure, but also during the total lifetime of the implant so-called *hematogenous seeding* of the implant by bacteria is possible, originating from infections at other locations of the body, such as skin, respiratory, dental, or urinary tract infections. For the first type of infections, the preventive antibacterial coatings are typically drug releasing coatings being depleted after 1-2 months contact with the host tissue (see description above). To prevent infections during the total lifetime of an implant, coatings or surface modifications which permanently will repel bacteria and enhance cell adhesion are interesting study objects. The complexity of the occurring bio-responses makes an important research effort essential to solve this medical issue.

5.7 Packaging trends

Wearable devices often need conformity to the body, and need to be small and thin, in order to provide the necessary wearing comfort to ensure patient compliance. Hence flexible or even stretchable electronic systems are needed, such realizations require dedicated material and technology developments to ensure high quality component and system packages. For electronic devices integrated into textile, washability is often an essential requirement, putting severe demand on the hermeticity of the device/component package. Reliability is important, multiple bending or stretching cycles should not result in material cracks, delamination of embedding polymers, etc.

In case of implanted electronics, packaging and integration differs even more from conventional practices for standard electronics. Biocompatibility and biostability are of utmost importance and are contextual properties, hence no ‘one-method-fits-all’ packaging solution exist.

Since the package of an electronic wearable or implantable device is forming the boundary between electronics and living tissue, two rather extreme worlds have to be combined, hence the development of such a package should be performed by multidisciplinary teams. Electronic engineers, material specialists, chemists, biologists, biomedical specialists and doctors, all have a useful role to play in the development of this very close interface between electronics and human organisms.

5.8 References

[1] H.A.C. Tilmans et al., Mult-sensors in SiGeMEMS technology, SSI (Smart System Integration), Amsterdam, 13-14 March 2013

[2] Daft, C.; Wagner, P.; Bymaster, B.; Panda, S.; Patel, K.; Ladabaum, I., "cMUTs and electronics for 2D and 3D imaging: monolithic integration, in-handle chip sets and system implications," Ultrasonics Symposium, 2005 IEEE , vol.1, no., pp.463,474, 18-21 Sept. 2005

[3] Report on Thin Wafers, Temporary Bonding Equipment & Materials Market, Yole Développement, October 9, 2012

[4] C. Landesberger, G. Klink, G. Schwinn, and R. Aschenbrenner, "New Dicing and Thinning Concept Improves Reliability of Ultra-Thin Silicon", International Symposium on Advanced Packaging Materials 2001, pp. 92-97, 2001

[5] S. Takyu, T. Kurosawa, N. Shimizu, S. Harada, “Novel Wafer Dicing and Chip Thinning Technologies Realizing High Chip Strength”, Proceedings of the 56th Electronic Components and Technology Conference, San Diego, CA, May 2006, pp.1623-1627.

[6] M. Tichem, M. Cauwe, Z. Hajdarevic, E. Kuran, B. Naveh, A. Sridhar and P. Weissel “Towards reel-to-reel integration of ultra-thin chips to polymer foils" Proceedings of the 4th Electronics System Integration Technologies Conference, Amsterdam, The Netherlands, pp.1-6, 2012

[7] E. Bosman, J. Missinne, B. Van Hoe, G. Van Steenberge, S. Kalathimekkad, J. Van Erps, I. Milenkov, K. Panajotov, T. Van Gijseghem and P Dubruel, et al. “Ultrathin optoelectronic device packaging in flexible carriers” IEEE JOURNAL OF SELECTED TOPICS IN QUANTUM ELECTRONICS., 17(3), pp.617-628, 2011

[8] J. N. Burghartz, W. Appel, H. D. Rempp, and M. Zimmermann, "A New Fabrication and Assembly Process for Ultrathin Chips", IEEE Transactions on Electronic Devices, pp. 321-327, 2009

[9] T-Y. Kuo, Y-C. Shih, Y-C. Lee, H-H. Chang, Z-C. Hsiao, C-W. Chiang, S-M. Li, Y-J. Hwang, C-T. Ko, Y-H. Chen. “Flexible and Ultra-Thin Embedded Chip Package,” 59th Electronic Components and Technology Conference (2009), pp. 1749-1753

[10] M.-U. Hassan, C. Schomburg, E. Penteker, C. Harendt, T. Hoang, J.N. Burghartz, “Imbedding Ultra-Thin Chips in Polymers,” STW ICT.OPEN 2011, Veldhoven, The Netherlands

[11] R. Dekker, M. Dumling, J.-H. Fock, 0. Gourhant, C. Jonville, T.M. Michielsen, H. Pohlmann, W. Schnitt, A.M.H. Tombeur, "A 10 μm Thick RF-ID Tag for Chip-in-Paper Applications", Proceedings of the Bipolar/BiCMOS Circuits and Technology Meeting, Santa Barbara, CA., pp. 18-21, 2005.

[12] M.-U. Hassan et. al, "Packaging Challenges Associated with Warpage of Ultra-Thin Chips", ESTC 2010, September 13 – 16, 2010, Berlin, Germany, in Proc. of 3rd Electronics System Integration Technology Conference, pp. 1-5, 2010
[13] "Industrial roll-to-roll inkjet printing of silver is feasible", Holst Centre press release, October 14, 2013
[14] J. van den Brand, R. Kusters, M. Cauwe, D. van den Ende and M. Erinc, "Flipchip bonding of thin Si dies onto PET foils: possibilities and applications," Proceedings of the 18th European Microelectronics and Packaging Conference (EMPC 2011), pp.425-430, 2011
[15] Chan, YC and Luk, DY, "Effects of bonding parameters on the reliability performance of anisotropic conductive adhesive interconnects for flip-chip-on-flex packages assembly II. Different bonding pressure," Microelectronics Reliability, vol. 42, No. 8, pp 1195 – 1204, 2002
[16] Jan Vanfleteren, Bjorn Vandecasteele and Tomas Podprocky, "Low temperature flip-chip process using ICA and NCA (Isotropically and non-conductive adhesive) for flexible displays application," Proceedings of the 4th electronics Packaging Technology Conference, pp 139 – 143, 2002
[17] Kay, R.W ; Stoyanov, S ; Glinski, G.P.; Bailey, C.; and Desmulliez, M.P.Y., "Ultra-Fine Pitch Stencil Printing for a Low Cost and Low Temperature Flip-Chip Assembly Process," IEEE Transactions on Components and Packaging Technologies, vol. 30, No. 1, pp 129 – 136, 2007
[18] K-L. Suk, H-Y. Son, C-K. Chung, J. D. Kim, J-W. Lee, K-W. Paik, "Flexible Chip-on-Flex (COF) and embedded Chip-in-Flex (CIF) packages by applying wafer level package (WLP) technology using anisotropic conductive films (ACFs)," Microelectronics Reliability, Volume 52, Issue 1, January 2012, Pages 225-234
[19] Marinov, V.; Swenson, O.; Miller, R.; Sarwar, F.; Atanasov, Y.; Semler, M.; Datta, S.; , "Laser-Enabled Advanced Packaging of Ultrathin Bare Dice in Flexible Substrates," Components, Packaging and Manufacturing Technology, IEEE Transactions on , vol.2, no.4, pp.569-577, April 2012
[20] M. Cauwe, B. Vandecasteele, A. Gielen, J. De Baets, J. van den Brand, R. Kusters and A. Sridhar, "A chip embedding solution based on low-cost plastic materials as enabling technology for smart labels," Proc 4th Electronics System Integration Technologies Conf, Amsterdam, NL, Sep. 2012, pp.1-6, 2012
[21] C. Bunel, S. Borel, M. Pommier and S. Jacqueline, "Low profile integrated passive devices with 3D high density capacitors ideal for embedded and die stacking solutions," Proc 4th Electronics System Integration Technologies Conf, Amsterdam, NL, Sep. 2012, pp.1-6, 2012
[22] SK Bhattacharya, and RR Tummala, "Next generation integral passives: materials, processes, and integration of resistors and capacitors on PWB substrates," Journal of Materials Science – Materials in Electronics, 11(3), pp. 253-268, 2000
[23] PL Cheng, SYY Leung, TW Law, CK Liu, JIT Chong, DCC Lam, "Quantitative analysis of resistance tolerance of polymer thick film printed resistors," IEEE Transactions on Components and Packaging Technologies, 30(2), pp. 269-274, 2007
[24] F. Egitto, R. Das, G. Thomas, and S Bagen, "Miniaturization of Electronic Substrates for Medical Device Applications," Proceedings of the 45th International Symposium on Microelectronics (IMAPS), San Diego, CA, US, pp. 186-191, 2012
[25] L. Godin, "Miniaturization of medical devices thanks to flexible substrates," 1st Advanced Technology Workshop on Microelectronics, Systems and Packaging for Medical Applications, France, 2012
[26] M. Kaltenbrunner, T. Sekitani, J. Reeder, T. Yokota, K. Kuribara, T. Tokuhara, M. Drack, R. Schwödiauer, I, Graz, S, Bauer-Gogonea, S, Bauer, and T. Someya, "An ultra-lightweight design for imperceptible plastic electronics," Nature, 499, pp. 458–463, 2013
[27] E. Beyne, P. Marchal, G. Van Der Plas, G, 2011 48th ACM/EDAC/IEEE Design Automation Conference (DAC), 5-10 june 2011, San Diego, CA, pp. 213.
[28] I. De Wolf et al. Microelectronics Reliability, Vol. 51 (9-11), pp.1856-1859, 2011.
[29] A. Redolfi et al. IEEE-CPMT 61st ECTC, May 31st – June 3rd, 2011 , pp. 1384 – 1388.
[30] A. Jourdain et al. IEEE-CPMT 61st ECTC, May 31st – June 3rd, 2011 , pp. 1122 – 1125.
[31] E. Beyne, Semicon West 2011 conference "3D IC Manufacturing – from concept to commercialization", San Francisco Mariott Marquis, San Francisco, CA, 12 July 2011.

[32] S. Priyabadini;T. Sterken;M. Cauwe;L. Van Hoorebeke; and J. Vanfleteren, "High-Yield Fabrication Process for 3D-Stacked Ultrathin Chip Packages Using Photo-Definable Polyimide and Symmetry in Packages," IEEE Transactions on Components, Packaging and Manufacturing Technology, accepted for publication, 2013
[33] Someya (ed.) "Stretchable Electronics", Wiley-VHC, ISBN 978-3-527-32978-6, Weinheim 2013
[34] Jan Vanfleteren, Thomas Loeher, Mario Gonzalez, Frederick Bossuyt, Thomas Vervust, Ingrid De Wolf, Michal Jablonski, "SCB and SMI: two stretchable circuit technologies, based on standard printed circuit board processes", Circuit World 38,4; 2012, 232-242
[35] Frederick Bossuyt, Jürgen Günther, Thomas Löher, Manuel Seckel, Thomas Sterken and Johan de Vries, "Cyclic endurance reliability of stretchable electronic substrates", Microelectronics Reliabilty 51, (2011), 628 - 635
[36] T. Sekitani and Takao Someya, " Stretchable, Large-area Organic Electronics", Adv. Mater. 22, pp. 2228–2246, 2010
[37] A. Romeo et al., "Elastomeric substrates with embedded stiff platforms for stretchable electronics", Appl. Phys. Lett., 102, 131904, 2013.
[38] Y.-Y. Hsu et al, "Novel Strain Relief Design for Multilayer Thin Film Stretchable Interconnects", IEEE Trans. Electr. Dev., Vol. 60, pp. 2338- 2345, No. 7, July 2013
[39] R Verplancke et al. "Thin-film stretchable electronics technology based on meandering interconnections: fabrication and mechanical performance", J. Micromech. Microeng. 22, 015002, doi:10.1088/0960-1317/22/1/015002, 2012.
[40] S. Xu et al., "Stretchable batteries with self-similar serpentine interconnects and integrated wireless recharging systems", Nature Comm., DOI: 10.1038/ncomms2553, February 2013
[41] D.-H. Kim et al. "Epidermal Electronics", Science 333, 838, DOI: 10.1126/science.1206157, 2011.
[42] R. Verplancke et al., "Thin-film based stretchable electronics technologies", Proc. SSI 2013 (Smart Systems Integration), Amsterdam (The Netherlands), March 2013.
[43] T. Linz et al., „Fully integrated EKG Shirt based on embroidered electrical interconnections with conductive yarn and miniaturized flexible electronics," in IEEE International Workshop on Wearable and Implantable Body Sensor Networks BSN 2006, Boston, 2006
[44] E. Simon et al., „Design and Optimization of an Injection-moldable Force-fit Module for Smart Textile Applications," in CIMTEC, Firenze, 2012.
[45] Ch. Kallmayer et a.l, „Large Area Sensor Integration in Textiles," in 8th international multi-conference on systems, signals and devices (SSD), Chemnitz, 2011.
[46] Inemi medical device project concerning medical electronic device testing, see: http://www.inemi.org/project-page/defining-requirements-development-medical-electronics-reliability-specifications
[47] Book edited by Buddy D. Ratner, Allan S. Hoffman, Frederick J. Schoen, Jack E. Lemons "Biomaterials Science: An Introduction to Materials in Medicine", Elsevier Academic press, 2004
[48] J. M. Anderson, Annu. Rev. Mater. Res., Vol. 23, pp. 81-110, 2001.
[49] G. Kotzar, M. Freas, et al, "Evaluation of MEMS materials of construction for implantable medical devices", Biomaterials, 23, 2002, pp. 2737-2750.
[50] Stöver T, Lenarz T. "Biomaterials in cochlear implants." GMS Curr Top Otorhinolaryngol Head Neck Surg. 2009; 8: Doc10, DOI: 10.3205/cto000062, URN: urn:nbn:de:0183-cto0000626
[51] B. M. Morcos et al., "Electrodeposition of Platinum Thin Films as Interconnects Material for Implantable Medical Applications" , Journal of The Electrochem. Soc., 160 (8) D300-D306 (2013); DOI: 10.1149/2.024308
[52] F. Mauron, "Encapsulating smaller and smarter implantables is a GLASS ACT", on line publication, http://medicaldesign.com/materials/encapsulating-smaller-and-smarter-implantables-glass-act
[53] M. Op de Beeck, K. Qian, P. Fiorini, K. Malachovski, C. Van Hoof, "Design and characterization of a biocompatible packaging concept for implantable electronic devices", Proc. of 44th Intern. Symp. on Microelectronics, Long Beach, CA, USA, Oct. 2011.
[54] M. Op de Beeck at al. "Improved chip & component encapsulation by dedicated diffusion barriers to reduce corrosion sensitivity in biological and humid environments" , EMPC 2013, Grenoble, France, Sept 2013.

Chapter 6 Communication & Data Storage

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6.1 Antennas and propagation

Antenna miniaturization and integration

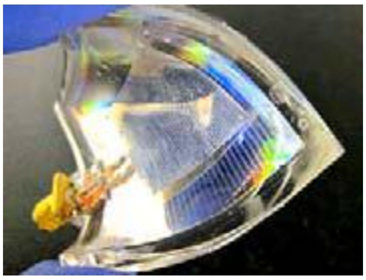
Future healthcare and wellness smart systems will rely on a wide range of wireless devices (handheld, wearable, implantable, swallow-able, injectable, etc.) with challenging size constraints. Since their operation frequencies are in the HF/UHF range, the antenna size and form factor are limited to sub-wavelength dimensions. In some applications (disposable devices, wellness applications), low cost is also a major requirement. In this context, the design of efficient antennas requires advanced miniaturization techniques and a close integration with the device package (see e.g. examples developed in the EU e-Cubes project [1][2]). An accurate knowledge/modeling of the device environment (including the human body), which strongly influences the efficiency, radiation and impedance of miniature antennas is also needed. Several concepts based on advanced materials (high permittivity, high permeability) and meta-materials have been developed recently to minimize the coupling between the antenna and the human body and thereby reduce the impact of RF losses in tissues and the variability experienced from the multiple usage scenarios. Flexible or stretchable materials (polymers, plastics, textiles) offer very good but very challenging opportunities for integrating antennas within clothes, bandages, and other similar supplies used for healthcare. Stretchability of the antenna results in shifting the operation frequency [3], however smart antenna design techniques can overcome this problem in some cases [4] .

Antenna-transceiver co-design and tunability

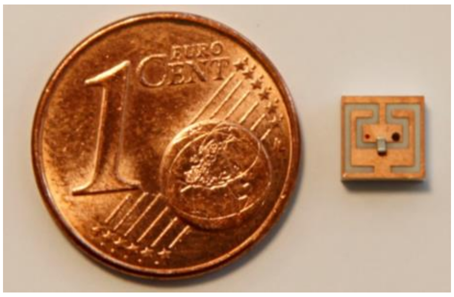
In contrast to the classical design methods relying on circuits (transceivers, switches, filters, duplexers) and antennas developed independently and with standard interfaces (50-Ω impedance, standard packages), antenna–transceiver co-design strategies have been successfully demonstrated to enable extreme antenna size reduction, better RF performances (Rx noise figure, Tx power added efficiency) and lower power consumption. This approach needs to be pursued and new design/simulation/optimization strategies are needed for a joint and global optimization of the radio front-end and the antenna. It requires integrated multi-domain (electromagnetic, thermal, electrical, system) simulation tools to leverage the multiple optimization parameters and access to all the systems requirements.

Tunability schemes at the transceiver or antenna level contribute to the miniaturization and the system performance by actively reconfiguring in real-time its characteristics (tuning frequency, antenna impedance, radiation) and adapting to the various usage scenarios (e.g. multi-standard compatibility) or environment variability. The efficient implementation of these schemes is a major bottleneck calling for advanced low-loss technologies (tunable materials, MEMS, NEMS).

Propagation around and through the human body
The propagation channel determines the main performances of wireless smart devices (range, data rate, QoS). A deep knowledge and understanding of its characteristics based on experimental and theoretical data are required to obtain representative antenna-channel models for a large field of applications and users activities. Radio channel models combined with bio-kinetics investigations could for instance offer novel features for localization and human activities monitoring systems.
Human tissues – wave interaction and propagation models over wide frequency range (from 10 MHz to 80 GHz) are required for wireless systems feasibility analysis. The understanding of the propagation modes in different frequency ranges could offer important link budget and coverage enhancements by opportunely choosing the operation band according to the application.
Finally, propagation models in multi-users and crowded environments are needed for interference characterization and mitigation.



(a)



(b)

Figure 6.1: Flexible two layers liquid metal antenna [5](a), ultra miniature frequency agile antenna for hearing aids [6](b).

EM exposure and dosimetry
EM exposure is a concern of increasing interest both for professionals, patients and citizens. Specific sensing and assessment techniques are required in future healthcare and wellness smart systems. The development of accurate, miniature, multi-frequency EM sensors and dosimeters will ensure the monitoring of EM exposure both in the lab and in the real field. Studies of new multi-standard receiver architectures and development of required critical integrated RF components are necessary to enable this function in future smart devices without detrimental impact on size, cost or power consumption. The development of innovative hardware or radio link optimization will be required with the objective to lower the EM exposure.

RF harvesting and charging for healthcare and wellness
As discussed in Chapter 2, RF can also be used for harvesting and charging of devices for healthcare and wellness. For more information, the reader is referred to this chapter.

6.2 Wireless solutions

Spectrum sensing
Wireless communications for wearable devices may be combined with spectrum sensing to improve the overall quality of service (QoS) and/or limit radiated power level of any single device. ISM bands may suffer from strong interference levels due to overcrowding. To guarantee QoS in these situations, transmitted power level should be increased but this may lead to a significant increase of power level consumption.

Alternative options may include the use of spectral sensing to estimate the most appropriate channel for the communication. The specificities of low power wearable devices in the context of smart healthcare and wellness systems should be considered in order to propose sensing techniques adapted to the specificities of the application: robustness, low resource and power consumption, adapted to specificities of the spectrum usage.

MAC protocols

Wireless communications for Body Area Network (BAN) have raised interest in modern applications such as smart fabrics and interactive textile, robotics, gaming and health. These technologies require specific investigations and optimizations to cope with a variety of application requirements and to limit radiated power, electromagnetic field absorption by the user, consumed power, device size and interference susceptibility. The propagation channel associated with BANs is slowly varying with the human motion, but the connectivity of the network may suffer from shadowing and fading variations due to the closeness of the human body and its environment. Some long fade states are highly probable in usual configurations. The vicinity of the human body is thus a challenging environment for the design of adaptable, dynamic and flexible BAN communication protocols with key requirements in terms of low power consumption, low latency and high reliability of communications.

A classical star network topology is unstable and experiences a time-varying Packet Error Rate (PER) probability which cannot be mitigated by retransmission mechanisms due to shadowing effects and slow variations of the channel. In contrast, relay nodes at different on-body positions experience different fading conditions and can mitigate both fast-fading and long-term shadowing using cooperative mechanisms with single or double-hop relaying. The main challenge in this domain is to develop self-organizing, adaptive and flexible MAC protocols automatically detecting the shadowing effects, quickly adapting the relaying scheduling to BAN changes, and making a trade-off between the quality of service and the energy consumption in real-time depending on the environment conditions and the user needs.

Security and privacy

Owing to the highly sensitive nature of the information handled by these healthcare and wellness systems, it is necessary to authenticate, authorize and account for accessing the data being gathered and processed. As a result, wireless communications in Body Area Networks are intimately associated to the identity of a person and may be vulnerable to security attacks. The following features of the wireless communication should be ensured:

- Availability: the communication service should be robust against service denial.
- Confidentiality: information should not be disclosed to illegitimate entities.
- Integrity: the integrity of the delivered message should be guaranteed.
- Authentication: nodes should be able to identify each other.
- Non-repudiation: a message origin may not be disclaimed.

What further complicates this effort is that different policies can be in place for normal and exceptional circumstances. For example, electronic health records should not be accessed by unauthorized people. However, in medical emergency situations first care responders should be provided with relevant information about the health status of the individual. Context-based privacy and security policies and enforcement may therefore be investigated. Of particular importance is the notion of privacy for these applications.
Different level of privacy may be considered:

- Selective Disclosure: the user may choose which attributes to disclose

- Un-traceability: the user identity should not be possible by back tracking of a credential.
- Un-linkability: it should not be possible to link different transactions/communications and associate them to a user.
- Predicate on attributes: ability to compute semantic data on attributes and to integrate them.
- Resource-light and power-aware security mechanisms adapted to wearable devices that may respond to these security paradigms.

Localization techniques (e.g. UWB)
Future health management systems will have to support precise localization and long-term tracking in daily-life environments. Provisioning accurate and reliable location information over time can indeed favour the development of more ergonomic, comfortable, less intrusive and highly reactive monitoring/prevention/rescue systems, in a variety of health and safety applications, such as:

- Early detection of critical situations (e.g., fall, fainting down…) for faster rescue and alarm launching;
- Physical rehabilitation at home through motion/posture capture or non-invasive and geographically unrestricted monitoring of the patient's activity;
- Assisted mobility for disabled or blind people;
- Finding people (e.g. trace elderly that are roaming about the nursery home).
- On the other hand, new applications necessitating the user's mobility or movement information have been also promoted in the fields of personal sports and fitness in order to:
- Optimize and secure the user's performance (e.g. offline jogging statistics about the overall travelled distance, peak and average speeds… possibly correlated with further physiological information);
- Enable self-learning of the good practice/gesture with quantified feedback (e.g. martial arts, skating).

From a technical point of view, the following unprecedented features are thus expected:

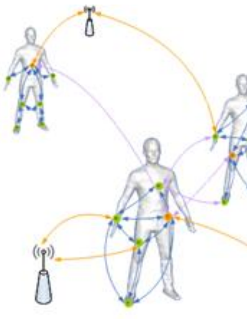
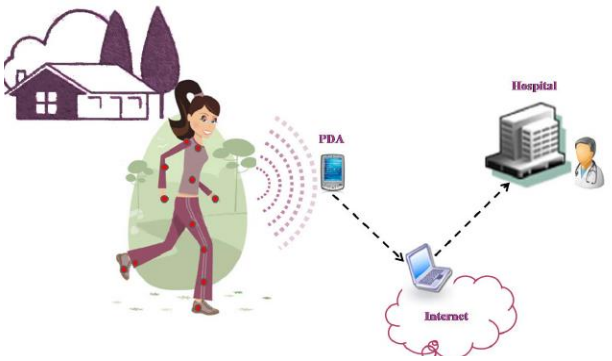
- Retrieve the real-time (time-stamped) trajectory of a mobile patient/user, possibly while collecting geo-referenced physiological measurements (i.e. as a function of the occupied position);
- Authorize self-learning of mobility patterns and personal habits out of the retrieved trajectories;
- Authorize detection of anomalies or unexpected events based on adequate decision tools;
- Augment indoor navigation capabilities through motion/posture capture with limited usage of extra and costly equipment at home;
- Ensure remote patient monitoring (e.g. from a distant hospital or medical centre).

In this context, numerous scientific challenges still have to be overcome to guarantee robust (i.e. with constant QoS), scalable and privacy-aware localization services:

- Location-enabled, low-cost and low-consumption integrated radio technologies still have to be improved to make possible scalable levels of precision and ranges (typically within sub-metric to centimetre accuracy at low data rates);
- In most GPS-denied environments (e.g. in residential houses or flats, in gymnasiums…) and for non-controlled operating conditions (e.g. device hold in the user's hand or pocket), propagation phenomena play a harmful role on the final localization performance. Relevant models or algorithms can benefit from e.g., the multipath

time/space correlation, or the sporadic nature of severe radio obstructions under mobility;

- Cooperation between mobile units or agents, as well as decentralized and/or multi-hop localization approaches, can be also beneficial, e.g. in case of stringent peer-to-peer range limitations and varying connectivity conditions, while exploiting user-centric and group/social mobility characteristics;
- Practical deployment/networking constraints (e.g. nodes' density, infrastructure-based vs. ad hoc, mesh vs. asymmetric topologies) as well as Medium Access schemes (e.g. cooperative ranging protocols and/or decentralized iterative positioning updates, both requiring packets' exchanges) support but impact the localization precision, synchronization requirements, and refreshment rates. Accordingly, cross-layer design approaches must be followed to ensure fine synergies between communication and localization means, while reducing their reciprocal impacts;
- As privacy is crucial for the collection of personal data, privacy-preserving location protocols must be put forward to limit the amount of location-specific information exchanged over public channels.

(a) (b)

Figure 6.2: Wireless localization exploiting different levels of cooperation within body area networks for joint motion capture and navigation applications [7] (a); wireless wearable health-monitoring and human locomotion tracking system [8](b).

Robust wireless system design for healthcare systems

General-purpose wireless systems such as Bluetooth or ZigBee do not include specific features to guarantee robustness and security required in healthcare and wellness applications. Dedicated standards for wireless body area networks, such as IEEE 802.15.6-BAN [9], provide quality of service differentiation (QoS), error correction, and security for sensitive data. IEEE 802.15.6, for example, supports traffic profiles for emergency messaging and strong security protocols for communications of sensitive medical information. On the lower stack of the protocols, it is important to implement techniques such as forward error correction code (FEC), bit interleaving, and cyclic-redundancy-checks (CRC) to detect and correct the impairments from the wireless channel. Initiatives to enhance robustness, and ensure the security of the wireless communication of healthcare data are important to make next generation wireless biomedical systems future-proof.

Wireless standards compliant design for healthcare systems

The Continua Alliance is a global group of companies and bodies seeking to promote the growth of the personal health market. Since the concern that incompatible systems will slow the roll-out of useful personal health devices, the Continua group focusses on ensuring interoperability. The Continua Alliance works with the IEEE standards association, where one of the earlier standards is the ISO/IEEE 11073 Personal Health Data (PHD) standard that addresses the interoperability of personal health devices (PHDs) such as weighing scales, blood pressure monitors, blood glucose monitors, etc. The IEEE 110073-200601-2008 document standardises the information profile of personal health devices into an interoperable transmission format so the information can be exchanged to and from personal telehealth devices and compute engines (e.g., cell phones, personal computers, personal health appliances, and set-top boxes).

In Europe, a recent initiative proposed to the European Standardization Body ETSI to define a new standard on Body Area Networks. The new standard focuses on a wide area of applications. The ETSI board approved the initiative by initializing a new Technical Committee **"Smart-BAN".** This TC will prepare ETSI deliverables for wireless Body Area Network for personal welfare. For the wireless communication part in healthcare systems, there are a few candidates that have their origin in the IEEE 802 wireless standardization group.

The first ones are the devices related to IEEE 802.15.4 Personal Area Network (PAN) standards. The ZigBee Alliance adopted the IEEE 802.15.4 standard, and one of their profiles is called ZigBee Health Care. ZigBee Health Care is a global standard for interoperable products enabling secure and reliable monitoring and management of non-critical, low-acuity healthcare services targeted at chronic diseases, aging independence and general health, wellness and fitness. The ZigBee products promote aging independence along with greater overall health, wellness and fitness awareness. A variety of the products offer a connection with health care professionals like doctors and nurses, allowing them to monitor users health even while they are at home. Continua has endorsed ZigBee Health Care as one of the low-power local area network (LAN) standard in the Continua 2010 Design Guidelines.

a) b) c) d)

Figure 6.3: Examples of popular wireless healthcare standardization initiatives: ZigBee-Health Care (a), IEEE 802.15.6-WBAN (b), Continua Health (c), Bluetooth Medical Device Profile (d)

Another wireless standard candidate for healthcare systems, and currently the most popular standard, is Bluetooth, initialized by IEEE 802.15.1 standardization work. Continua Health Alliance version 1 design guidelines include Bluetooth communication. Other IEEE wireless related standards for healthcare are the medical body area network standard 802.15.4j-MBAN, the Chinese medical band standard 802.15.4n-CMB, and the wireless body area network standard 802.15.6-BAN. Finally, a popular wireless protocol for sport, wellness and home health is ANT+, which is an interoperability function that can be added to the base ANT protocol (a proprietary wireless sensor network technology) [10]. It is targeted at manufacturers of "bike computers, diagnostics, power meters, heart rate monitors, etc." and promoted by the ANT+ Alliance. It is important to monitor and contribute to existing and upcoming wireless healthcare standards to ensure interoperability between devices.

6.3 RF IC design

Low-power RFIC design and architectures on advanced silicon technologies

RF solutions in the future will benefit from the high performance of the FD-SOI technology and its efficiency in terms of power consumption. This will help to integrate powerful, but low-power, digital process with high performance analog front-end [11]. There is a strong challenge here to push electronic systems to higher power efficiency as transistors can run about 30% faster than with traditional CMOS and are about 50% more efficient in terms of power consumption, at a much lower leakage level. In addition, operations at low voltage below 0.5V, currently investigated for larger CMOS node size [12]-[14] are made easier and will help major power consumption savings. The target in terms of power consumption for the RF front-end dedicated to Wireless Sensor Networks lies below 1 mW. Integrating more digital processing with the analog front-end will help to introduce more flexibility in the real-time performance RF IC by always considering the best sensitivity / linearity / output power required to correctly operate a communication. These extreme power savings demanded by the WSN world will benefit to the global telecom market as new IC design trend will arise.

Ultimately, RF solutions will have to combine protocol high-level considerations and RF front-end possible optimizations to make a complete network really efficient. Sense the environment and thereafter react accordingly will be made possible thanks to digital-oriented front-ends [15]. Therefore, a strong effort in this direction is required to get the best from these new technologies, creating a real breakthrough in IC design. From a cost point of view, the development of the Internet-of-Thing (IoT) will make production volumes for low-power/low-cost RF front-end grow dramatically in the future. Thereby, mastering short CMOS transistor nodes for analog front-ends is required to decrease the overall cost of RF links.

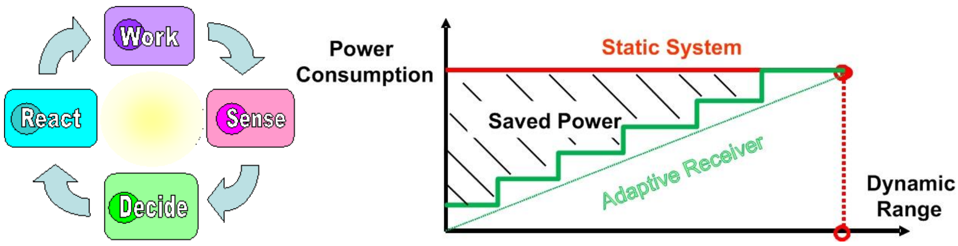


Figure 6.4 : Sense & React concept: dynamic of the receiver front-end adjusted in real-time.

Antenna-transceiver co-design

Multi-standard and multi-band accesses are key features in the future, as spectrum sharing is a crucial point in telecom applications as well as in WSN ones. This makes the air interface very complex to be designed: a variety of filters and antennas, broadband design of RX and TX front-end etc.. . Techniques to reduce the complexity and loss in performance due to this trend must be studied and massively deployed into the IC design community. Promising approaches for this are considering matching the antenna impedance to the RF front-end, most likely at a different interface impedance level not equal to 50 ohms. To do so, the transceiver should always know the conditions in which the antenna is operated, which of course includes the knowledge of the band and frequency in use but also the environmental conditions, which greatly impact the antenna behaviour. So, sensing features must be added to the front-end as well as a processing unit to better match the antenna to its active companion IC [16]. New paradigms of multiple antennas, including MIMO schemes, also go in that direction, of even more complex coupling between the RF IC and the radiating elements.

Polymer RF electronics

Wearable devices should be comfortable to wear and robust enough to operate under realistic wearing conditions. Ideally, the wireless sensors and actuators involved should be included in the fabric, so that the wearable device becomes washable, water proof, easy to install and operate by the user, often a patient. Once it is put on, it should turn on automatically, create the needed connectivity and start collecting data and performing the desired actions. We foresee that, apart from the possible avenues sketched elsewhere in this document, polymer electronics (also called organic or plastic electronics) will become a viable alternative to silicon-based technology, but only when it is able to improve on reliability, low power operation and operating speed. Apart from being used for transistors, polymers could also serve as an excellent base material for sensors, displays, backup batteries and antennas, basically creating a one-stop shop for everything needed to build the next generation of wearables.

Heterogeneous integration

Innovating stacking of technology leads to greater integration, in order to reduce the form factor of RF systems. It also helps to optimize power consumption and enable long-term functioning of hand-held systems as traces between various IC are reduced, limiting the parasitic capacitance and the associated added consumption. Ultimately, integration of RF Front-End (RF FE) on single-chip IC with of course all the digital process and the application support, like μC, is a must-have, but co-integration with filters, resonators, passives, phase shifter and antenna matching must be considered as a future enabler for lower form factor, better production yield and not the least reduced power consumption [6] .

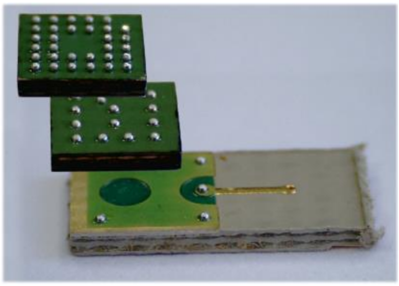


Figure 6.5 : Smart-System IC modules for miniaturized RF communications (courtesy of EU FP7-WiserBAN project [6]).

Integrated Soc Design

Miniaturizing transceivers, by single chip design, is attractive for industry. Except the low-cost aspect of minimum die size, it also helps for ultra-low power operation by avoiding power hungry high-speed I/O interfaces. Integrated SoC design can also help in fast synthesizer locking, and minimizing transmit-receive switching time. Excluding expensive RF IC technology options and minimizing external components, needs careful analysis of the available architectural choices. Without proper analysis of the pros and cons of certain architectures, it is difficult to obtain high performance of the transceiver.

6.4 Data Processing & Storage

6.1.1 Data Processing

There are a variety of biomedical applications, ranging from low-speed ECG beat detection, up to high speed multi-lead EEG seizure prediction. In ECG, only every few seconds data needs to be analysed by the processor. This analysis usually requires a very short period of time. In EEG, (relatively) large amounts of data from many different channels need to be analysed. This requires much more performance from the processor. Processor systems need to support this wide range of bio-medical applications, but also several aspect of communication protocol handling. The overall targets for a biomedical processor system lead to energy-efficiency and scalability demands:

- The design of a processor architecture system that can execute compute-intensive algorithms in an energy-efficient way. Also, energy efficient memories and memory architectures are critical, since in low-performance applications (like ECG), the energy consumed by memory can be more than 90%.
- To have a processor system that is scalable in performance, voltage, and frequency to allow both energy-efficient executions of low-performance as well as high-performance applications.

Topics in biomedical data processing are:

- Multi-core systems for energy efficiency
- Dynamic performance scaling, e.g. smart power gating
- Dynamic frequency voltage scaling, e.g. based on in-situ performance monitoring

A more detailed discussion on the sensor data processing aspects for biomedical applications are detailed in chapter 4 of this document. Below the communication and storage related aspects of data processing will be discussed in more detail.

Generic versus dedicated processors

Generic low-power microprocessors typically need only little energy per clock cycle. However, the number of cycles such a processor needs for executing signal processing tasks is very high compared to DSP alternatives. The main reason for this is that the instruction set of these processors are tailored for control code and not for digital signal processing algorithms.

However, mapping applications to an alternative processor is very time consuming and therefore costly. Also, the maintainability becomes difficult since these alternative processors typically require very specific code modifications to enable an efficient implementation, which are neither portable to any other platform nor understood by the general compilers running on the workstations. Especially in the context of wireless protocol processing, flexibility for changes in standards and /or application layer software is often needed. This favours general purpose low power purpose processor solutions due to the relatively easy adaption to such changes.

Solutions that provide the best of both worlds are being asked for, specifically designed to increase the power efficiency of biomedical signal analysis applications. The main application could be still mapped on a generic processor, but the digital signal processing blocks are off-loaded to task-specific hardware-blocks, also called accelerators.

Data compression and communication

While in many practical use cases there is a high interest to transmit sensor raw data (containing full sensor information) to from a local sensor attached to the body of a patient to a central storage hub (like a smart phone, or a main computer at home doctor's office), this is often not an energy efficient solution. Communication, but especially radio transmission is the most energy consuming task in such systems. Therefore reduced communication can save considerable amount of energy at places where this is an important system requirement (e.g. see introduction 6.1). Therefore there are two ways to reduce communication energy: reducing the amount of data being communicated and reducing the timely frequency of communication events. Energy efficient compression algorithms and low power communication schemes in the context of medical sensor data transmission are therefore an interesting topic for future research.

Source Coding and Error protection.

To improve the reliability of wireless Ultra-Low Power (ULP) transmission of ExG biomedical signals, exploitation of the correlation between the multi-lead electrodes can be an interesting topic for a reliable yet power-saving solution. Mathematical models have to be developed that describe the correlation of the temporal, spatial, and signal representation dimensions. The amount of transmitted data can be reduced by extracting the most significant components (see section 4.6). Channel coding can be applied at transmit side to mitigate wireless channel impairments. At receive side, the mean square error can be minimized by analysing intra-channel continuity, smoothness, and similarity.

Another topic is to improve data recovery from wireless channel noise and interference. This could be done by adopting the signal redundancy to recover signal from noise. In the receive part, the linear prediction method LMS uses the received bits in nearby time slot, channels and bit planes. However, the performance of LMS is highly related with actual bit distributions. Therefore, a strategy that recovers the most significant bit errors only would be an interesting way forward.

The saved radio power consumption applying the above-mentioned methods could be used to add channel coding. An example is the repetition codes at low SNR to lower the bit-error-rates and the packet-error rates. At high SNR, a Reed-Solomon (RS) code could be a good choice.

6.1.2 Storage

Storage challenges in biomedical applications are split into two classical use cases. First, the software or application code for the application needs to be considered. Here the stored data is control code for tasks like communication control, triggering measurements, or for doing data processing. Second a local repository for biomedical data is needed. These two use cases also have different requirements for the memory properties.

Code data need to be read out fast and at lowest energy per bit. Code still needs to be available after a power loss or shortage. The usage of non-volatile memories is therefore mandatory. For a certain amount of flexibility and the possibility to do software updates at a later point in time (in the field) the memory should be more than one time programmable. Today in most practical implementations flash memories are used here. Just recently several other non-volatile memories have been emerging. These are namely FRAM, MRAM, and a couple of different types of phase change memories. These memories may be considered as promising future alternatives – in especially if they allow energy efficient reading and writing of non-volatile data at reasonable system cost.

Data memory is mostly needed in biomedical applications to locally store sensor information or user data. While it is desirable to store this information beyond a potential power loss it is not mandatory in all use cases here, however writing of data into the memory happens more often compared to code memory. Therefore SRAM today is mostly used as a more energy efficient alternative here. This is especially a good choice in applications cases data only need to be stored temporarily for intermediate calculations or data compression before wireless transmission. Here architectural or design techniques to reduce both active read and write energy, but also and especially leakage currents during data retention periods will be challenges which have to be overcome for future biomedical systems. Since leakage does not scale well with modern CMOS process nodes this topic has to be addressed by further research. Potential solutions are the use of low voltage, write assisted SRAM cells, but also the usage of emerging non-volatile memories for energy efficient data storage. Those memories do not need to be powered down during sleep modes while still conserving the information for the system.

Energy efficiency, cost efficiency, but also safety and security needs to get further evaluated to find out which type of memory and memory partitioning best serves the application level needs:

This start at the architectural level with a trade-off between more distributed local storage at the sensor node or more data communication and related data storage on smart phone, computers, or centralized servers.

Memories typically dominate the chip area and therefore also the cost of integrated SOCs. Due to the desired wide-spread usage of such chips in the aging population, for biomedical applications memories need to be designed to be cost effective. Cost constraints are translating into technical requirements for efficient bit cell structures and low control overhead at a high production yield of both. This requirement therefore will include energy and cost efficient redundancy concepts. Besides cost, the energy efficiency for reading and writing data today is the main technical challenge. Circuit-level innovations in local architecture are being asked for. Examples are energy efficient hierarchical bit-lines structure including includes low swing global bit-lines and half-supply pre-charged short local bit-lines. Innovative calibration techniques with the use of global read sense amplifiers of the memory blocks not only adds to the variability resilience but also yields maximum energy reduction compared with existing calibration techniques.

Finally there is a growing desire to have access restrictions to both code and data for security and safety reasons on the application level. Safe and secure memory data read-out and related memory controller architectures will become a must for wide adoption of biomedical systems in future health care concepts.

Conclusion

Data processing, storage and communication are essential functionalities of future smart systems; their use in healthcare and wellness applications requires a very high level of integration for these devices to be worn on, or implanted in the human body without impact on the activities they have to monitor and no discomfort for the patient/user.

Regarding compactness and integration, hardware elements of the system such as antennas, sensors, integrated circuits, energy harvesting devices and the integration technologies used to assemble them are of prime interest. These integration constraints as well as the very specific operational environment of healthcare and wellness applications trigger some challenges in terms of wireless communications between these smart systems, whether they operate in networks or as stand-alone systems. There is a strong first need for communication protocols that guarantee both a high level of robustness and energy efficiency, but also security and privacy. Wireless communication systems shall also support radio-localization functions, which will enable a wealth of novel applications. The standardization activity in this area is very important to ensure the level of performance and interoperability expected from these systems.

6.5 References

[1] R. van Doremalen, P. van Engen, W. Jochems, Shi Cheng, T. Fritzsch, W. De Raedt, "Miniature wireless activity monitor using 3D system integration," *2009 IEEE, International Conference on 3D System Integration (3DIC)*, pp. 1–7, 28–30 Sept. 2009.

[2] FP6 e-Cubes project, www.ecubes.org.

[3] Q. Liu, K.L.Ford, R. Langley, A. Robinson, S. Lacour, "Stretchable antennas," *2012 6th European Conference on Antennas and Propagation (EUCAP)*, pp. 168–171, 26–30 March 2012.

[4] A. Arriola, J.I. Sancho, S. Brebels, M. Gonzalez, W. De Raedt, "Stretchable dipole antenna for body area networks at 2.45 GHz," *IET Microwaves, Antennas & Propagation*, vol. 5, no. 7, pp. 852–859, May 13, 2011.

[5] G.J. Hayes, *et al*., "Flexible liquid metal alloy (EGaIn) microstrip patch antenna", *IEEE Trans. on Antennas and Propag.*, vol. 60, no. 5, May 2012, pp. 2151-2156.

[6] FP7-Wiserban project, www.wiserban.eu.

[7] J. Hamie, "Contributions to Cooperative Localization Techniques within Mobile Wireless Body Area Networks", *PhD dissertation*, University of Nice–Sophia Antipolis, Dec. 2013.

[8] H. A. Shaban, "Novel Highly Accurate Wireless Wearable Human Locomotion Tracking and Gait Analysis System via UWB Radios", *PhD dissertation*, Virginia Polytechnic Institute and State University, April 2010

[9] www.ieee802.org.

[10] http://en.wikipedia.org/wiki/ANT%2B - cite_note-WhatIsAnt.2B-1

[11] Y. Ming-Ta, *et al*., "RF and mixed-signal performances of a low cost 28-nm low-power CMOS technology for wireless system-on-chip applications", *2011 Symp. on VLSI Technology*, Honolulu, HI, June 14–16, 2011, pp. 40–41.

[12] A. Saito, *et al.*, "An all 0.5V, 1Mbps, 315MHz OOK transceiver with 38-μW career-frequency-free intermittent sampling receiver and 52-μW class-F transmitter in 40-nm CMOS", *2012 Symp. on VLSI Circuits*, Honolulu, HI, June 13–15, 2012, pp. 38–39.

[13] T. Matsubara, *et al.*, "An 0.5V, 0.91pJ/bit, 1.1Gb/s/ch transceiver in 65nm CMOS for high-speed wireless proximity interface", *2011 IEEE Radio and Wireless Symp. (RWS)*, Phoenix, AZ, Jan. 16–19, 2011, pp. 74–77.

[14] A. Shikata, *et al.*, "A 0.5V 1.1MS/sec 6.3fJ/conversion-step SAR-ADC with tri-level comparator in 40nm CMOS", *2011 Symp. on VLSI Circuits (VLSIC)*, Honolulu, HI, June 15–17, 2011, pp. 262–263.

[15] A. Oguz, D. Morche, C. Dehollain, "Adaptive power reconfigurability for decreasing power dissipation of wireless personal area network receivers", *2011 IEEE Int. Symp. on Circuits and Systems (ISCAS)*, Rio de Janeiro, Brazil, May 15–18, 2011, pp. 1900–1903.

[16] Q. Gu, A. S. Morris, "A New Method for Matching Network Adaptive Control", *IEEE Trans. on Microwave Theory and Tech.*, vol. 61, no. 1, January 2013, pp. 587-595.

Chapter 7 User Interface & Acceptance

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7.1 Introduction

User interfaces to appliances and technical solutions are key to developing solutions for *people*. These interfaces between the human and the machine enable exchange of data, information and, finally, the generation of knowledge. Interfaces

There are different constraints on interfaces depending on which criteria are applied: If one looks at interfaces from a security and safety perspective, they should be as narrow as possible – the surface area that is exposed to a potentially harmful influence. However, if one looks from a more human perspective, interfaces should be wide and robust, allowing for a variety of inputs leading to a desirable output. In the case of user interfaces, different diverse modalities also are important. This latter view is the one which will be adopted in this chapter primarily. We take a positive stance here: User interfaces should enable, not restrict.

A user interface is a key ingredient in tools that address human needs and amplify human capabilities. Furthermore, a user interface helps converting what users potentially can do into what they want to do.

7.2 User interfaces

User interfaces that are accessed with our hands are and will be most important they have some of the densest areas of nerve endings on the body, and not just sensorial capabilities but also tactile means – in short, all ingredients for efficient and deep interactions. Nevertheless, in this section, we will look beyond hands as primary means for interaction especially when it comes to multi-modality and exploiting unusual capabilities of sensing and acting.

7.2.1 New Interface Paradigms and Modalities

While the basic modalities of human computer interaction have been explored thoroughly in the past years, combinations of modalities and multi-modal interaction as an interaction paradigm have a big future when it comes to small, wearable and often concealed devices in the body area. Also new technologies will make better and more sophisticated interaction modalities possible, such as Google Glass[1], Leap Motion and voice-based interfaces (see below) have been enabled by recent progresses in engineering. Speech combined with gestures (multi-modal interaction EITICT labs, DFKI) is one example that illustrates how in the future devices can be directed by composed user inputs and how robust interfaces need to be developed to support layered human input, and even contextual reasoning to work with ambiguous input from more than one modality. Future users will be more versed in the different “dialects” of interaction, for instance, be fluent in interacting with devices via speech, and similar to driving a manual car, operating on different modality layers will be more natural the more these modalities are embedded into everyday use.

A good example is the increased usage of speech interfaces. During the past decades great progress has been made regarding the syntactic problems of speech recognition (syllable recognition, word separation etc.) but the widespread application of speech interfaces still did not happen. The main difficulty nowadays is interfacing at a semantic level: relating the spoken utterances to the real world. It is no surprise that semantic web technologies and ontologies are the focal point of contemporary developments in applying speech interfaces. An example is the smartWeb project at the German Research Centre for Artificial Intelligence (DFKI) in Saarbrücken, Germany (Figure 6.1). In this system bio-signals are also being used to recognize the state of the user.

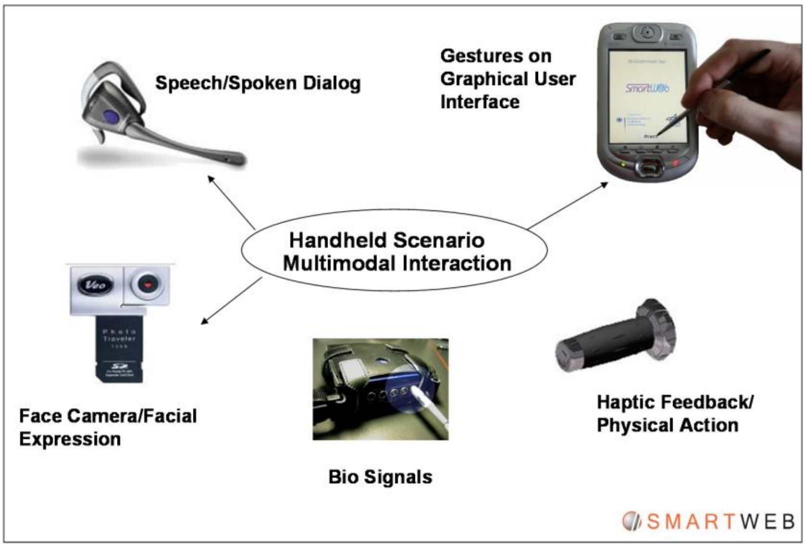

Figure 7.1: The multimodal dialog handheld scenario comprises spoken dialog recorded by a Bluetooth microphone, gestures on the graphical PDA touchscreen, and camera signals. In addition, the SmartWeb project uses recognition of user state in bio-signals to adapt system output in stressed car driving situations and haptic input from a force-feedback device installed on a motorbike [12]

Multimodal interfaces using speech are already becoming attractive for medical expert user interfaces. A good example is the RadSpeech semantic dialogue system for radiologists. Again, the main progress is coming from semantics: the system includes an ontology-based dialog platform. RadSpeech is part of the THESEUS MEDICO project which is funded by the Federal Ministry of Economics and Technology and where trials are done in cooperation with Siemens and the University Hospital in Erlangen (Figure 7.2).

Commonplace modalities like tangible interfaces, touch, gestures, speech and others will be complemented by human signaling that is picked up by sensors specialized for certain body postures required for particular human activities (driving, riding, sleeping, human contact). These can be more subtle ways of signaling than what is available today as sensors and human adaptation to having sensors in strange or at least unusual body regions or postures need to further develop. At the same time, sensors will develop from mostly single purpose measurement instruments towards more integrated multi-measures, which allow for sensing in multiple modalities, but also to combine two sensors to raise the accuracy of a single measurement. Even intentionally deactivating and using certain modalities only in specific case might a possibility to be exploited more in the future.

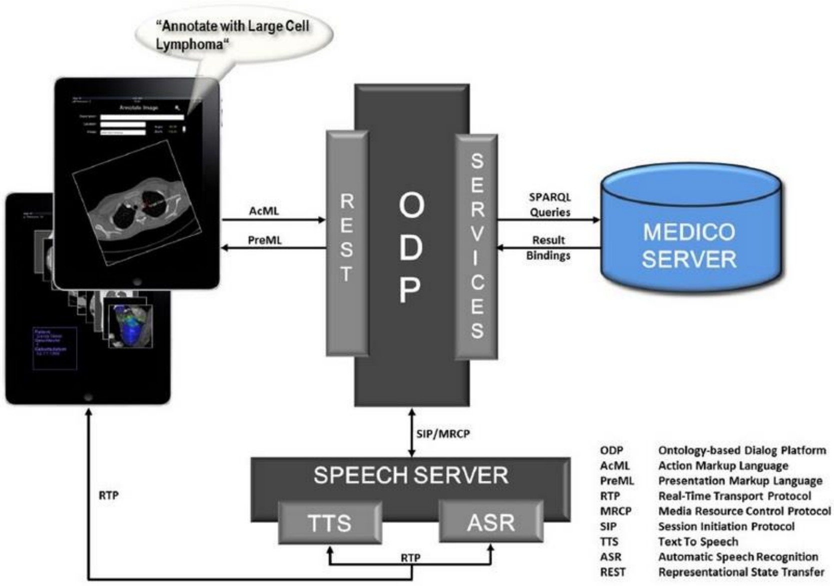

Figure 7.2: Overview of the RadSpeech system for radiology [12].

Perceiving collected data will develop from explicit means such as alphanumeric small displays, dashboards and visualizations towards information decoration and more ambient and (conceptually) better-integrated "displays" of collected data. An interesting area of research in this sense is *peripheral awareness* of information presented in the environment and the human body. This is based on the fact that human cognitive means to process information are clearly limited, and although people actively push the frontier of what and how much they can process, there are limits. Peripheral awareness is based on the notion that not all information needs to be perceived in the centre of attention: often it is better and more efficient to place information in the peripheral of, for instance, the visual field to leverage human information processing capabilities better. Such data is only drawn into the centre of attention when subconscious processes indicate a need for higher level of cognition - and attention.

Similarly, peripheral manipulation can be a means to unobtrusively interact with devices close to the human body, which happens already nowadays, for instance, when subconsciously playing with an object in a coat pocket – but this is currently not exploited as a valid and credible means of interaction.

7.2.2 Simulation and Games

When motivation is a scarce resource, go for self-image or competition. Along these lines, end-users' motivations to wear devices that might be tedious to affix, cumbersome to wear all day, strange looking, or simply decrease the perceived self-value of users, can be boosted by turning these device into playful or even "cool" personality attributes.

In the future, tracking oneself and gathering data will more and more become an essential element of games that take place in the human reality – not in virtual spaces projected by video games. Game developers will increasingly reach out to new means of getting players' inputs and using those to derive ever more challenging, immersive and real-feeling game plays. While games drive the need for data, data tracking could be motivated by casual games or small challenges, while still maintaining the general context and purpose of health or wellness related data.

Gathering data during usual daily activities is currently still not openly publicized and shown off, but will be more becoming an attribute of one's personal lifestyle – especially if this trend is picked up more by influential players in the fashion and consumer electronics areas.

Visualizing medical data, sensor data and visualizing internal hidden aspects of our own bodies is a great tool for increasing awareness. The most obvious contemporary examples are body weight simulators, where exercise and eating are translated into BMI numbers and visualizations thereof. Clearly these simulators will become more attractive and more persuasive once real-time data are added. This is an example from the area of persuasive technology (the aim is not just measuring data, but helping the user to adhere to a behavioural strategy which is easy to explain but hard to execute). It will not take long before elements of the SIMS game and body-weight/body appearance simulators will be combined (Figure 7.3 [13]).

Figure 7.3: Weight Loss Diet Simulator Calorie Calculator BMI BMR Tool Counter iOS app [13]

Technology to combine external and internal body images is not only a great tool for increasing awareness, but even for professional training of medical doctors. An example is the Mirracle system (Figure 7.4), developed by a consortium including the Technical University of Munich, where one can "look" into one's own body. The body posture is obtained from a Microsoft Kinect and the visualization of bones or other structures is taken from a 3D image of the user, like CT or MR. This could be a great platform for adding even more real-time sensor-based body information. Although the Mirracle does not come with the usual competitive performance elements of gaming, other medical training games *do*, for example in laproscopy.

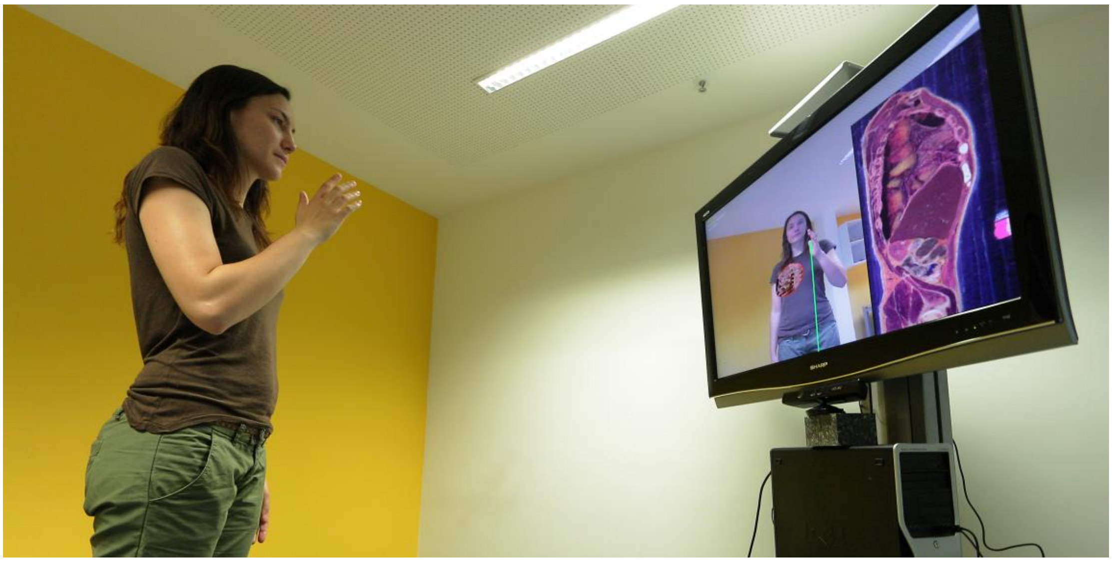

Figure 7.4: Mirracle, an augmented reality magic mirror system [14]

7.2.3 Lifestyle and Wearables

Wearable sensors and information displays naturally relate to garments, fashion and similar means for self-expression and lifestyle. Health-related applications that integrate with garments will be accepted easier by future consumers and users for a few reasons: (1) they blend into their lifestyle, become invisible and do not cause stigmatization, (2) new fashions always afford a transition of style or mindset which allows for "piggy-back" transitions in wellness and health-care applications, and (3) information can augment garments in new, unforeseen ways – even dynamically.

An important development is that garments are designed to act as an information display to present personal data. Here are two examples: the Flip Dot Dress by Van Dongen and Schatzmayr and the Drapely-o-lightment dress by Toeters and Feijs (Figure 7.5). The flip-dot dress by Pauline van Dongen and Daniel Schatzmayr was presented at the End Symposium of the Technosensual Exhibition, curated by Anouk Wipprecht in Vienna. Six hundred flip-dots are covering the upper part of the body. The garment is constructed of a layer of foam and neoprene, both laser cut. A small PCB board is integrated in the dress.

Drapely-o-lightment by Loe Feijs and Marina Toeters is a skirt created as an exploration into the integration of electronics and garment. The design takes into account not only the inclusion of squares in the visual design, but also the tactile and visual properties of hard components in a traditionally soft medium. Drapability and light are the two design themes of this skirt. The light sources used are OLEDS (Organic light-emitting diodes). The OLEDS fade in and out in the breathing rhythm. But if the sensors perceive action, it shows the heartbeat. The skirt is an example of the idea that light sources in wearables can be used as a means of self-expression and communication.

What is currently being done for garments and fashion items naturally extends to the packaging of sensors and worn information displays that are not integrated into clothes, but still worn during the day close to the body: the form giving and interaction should be non-threatening, sensual and reduced to the immediate functionality. There is a preference for "calm" technology that acts in the periphery of attention and makes use of pull mechanisms rather than pushing information content to the user at any point in time.

Figure 7.5: Flip dot dress information display (www.paulinevandongen.nl/) on the left side, Drapely-o-lightment (gallery.bridgesmathart.org/exhibitions/2013-bridges-conference/feijs) on the right

Sensors and corresponding information displays will deal with dynamic data that reflects the user's life on certain levels. This content needs to be presented in form and interaction that makes sense to the user in different situations of daily life. Therefore, information displays need to adapt to what the user is currently doing, which can result in the need to change the shape of the sensor enclosure or display, changing the accessibility of information, bringing in new contextual data, or representing the data in a more appropriate form for a new social context (cf. Privacy).

7.2.4 Connectivity and Remote Action

Ever increasing coverage of mobile data plans, reception and even city-spanning Wi-Fi networks allow for permanent connections, data streaming and fast round-trips to remote processing units. Real-time data will be a core requirement on future devices and services, but not just the delivery of such data in a fast pace will matter, also expectations of consumers and professional stakeholders will develop such that faster reactions on these data will be expected. In interaction design, 100ms is the threshold for perceiving a reaction as "instant"; a similar measure exists for the perception of responsiveness of websites and web services. All data-related services will eventually have to abide to these principles as well – with infrastructure not just enabling faster sensing and bandwidth, but also faster acting based on personal processed data.

Interfaces will mediate these expectations by setting the pace and providing fallback solutions in case signal reception is low or remote services are unavailable. A growing area of user interfaces will be developed for managing and utilizing remotely monitored implantable devices. An example is the CareLink® system developed by Medtronic. The same radio link technology and data transmission protocols can be used for a variety of implants and devices, such as: Continuous Glucose Monitoring (CGM), Insuline Pump

Therapy, ICDs (Implantable Cardioverter Defibrillators), CRTs (Cardiac Resynchronization Therapy Devices) and ICMs (Insertable Cardiac Monitors).

For example, the functionalities used by the health care professionals in the cardio rhythm area include in-clinic access to heart failure diagnostic data, remote monitoring services and databases, an in-clinic wireless cardiac device programmer and device follow-up system that integrates demographics, scheduling, and cardiac device data.

With increasingly more and more data becoming available, a main worry is not to create more workload for health care professionals. It is expected that the user interfaces will be PCs or even workstations equipped with large screens dedicated software to access and visualize more and more data. Typical present-day user interfaces are designed as report generators, producing a wide variety of charts such as Data Export Reports, Daily Summary Report, Data Table Report, Device Settings Report, Logbook Diary Report, Modal Day Hourly Report and so on (this is for the CareLink® Personal). User Interface progress has to come from the fields of Data Visualization, Data Mining and Info-graphics. The data will be coupled to financial systems (billing for the services) and research databases (essential in evidence based medicine) and other Hospital management systems (for scheduling and sharing information among health-care workers).

Whereas the cardiac devices are mainly aimed at providing data to the health care professionals in the clinic, the Continuous Glucose Monitoring has also a dedicated user-interface for the patient him/herself, called CareLink®Personal (Figure 7.6). The patient's user interface has to be simpler than the professional's because the devise is supposed to be a tool empowering the user while being integrated seamlessly in daily life activities. Again, typical screens are reports, but less technical than the typical healthcare workers reports. Here is an example:

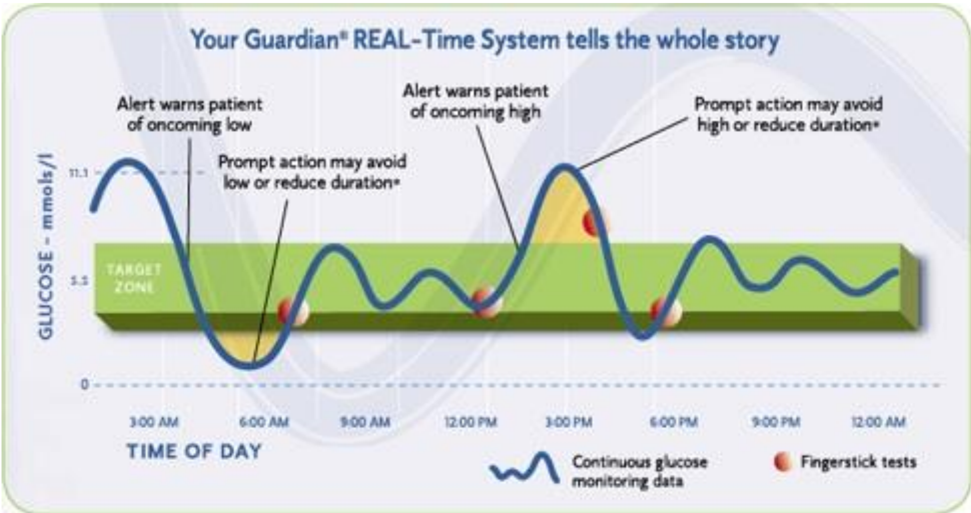

Figure 7.6: Guardian REAL- time System, http://www.medtronic-diabetes-me.com/Guardian-REAL-Time.html

Although nowadays there are still dedicated physical devices or special boxes, both serving as a hub in the communication links and as an information display, it is to be expected that these devices disappear and that the smart phone is the main hub and the main information display. User customization is becoming important as well, not only for the user-interface, but also for the form giving of the devices and accessories. From an advertisement: "Express yourself! Let your Medtronic device reflect who you really are. Choose from hundreds of fun designs or create your own customized skin."

(www.medtronicdiabetes.com/treatment-and-products/insulin-pump-style-and-accessories)

Implants and medical devices are leaving the pure medical domain and become a mixed medical/lifestyle phenomenon. Doubtlessly these user interfaces will also become connected to social-media where users can share their worries, small and personal achievements, disappointments, etc. and comment on it. The privacy and security risks are high, but some people might be willing to take risks.

7.2.5 Professional Stakeholders

Consumers and end-users will not be the only ones accessing the content, as it will be generated by sensors and devices close to the human body. Professional users are important stakeholders of healthcare and wellness related data, as they have the expertise to diagnose, detect patterns and interpret the data given their training and day-to-day practice. One can assume that those professionals will be able to deal with more data, higher level of details, more complex mappings of sensors to displayed data and some understanding of the algorithms that lead to data presented on the user interface. The context of use will be different, and most likely remote to the user and worn sensors. Healthcare is moving towards a more casual and explicitly remote appliances that measure 24/7, process data with powerful built-in hardware-accelerated algorithms, store the data in a cloud-base storage facility and then allow healthcare professionals to access this data from their workplace, given desktop or tablet computers – or even dedicated devices.

7.2.6 Existing Development on User Interfaces

In [4], a user interface layer is reported to bring device independence to users of AAL systems. Many ICT services older people could derive a benefit from lack of accessibility, adoptability and usability of the user interface concerning arising special needs specific for the target group. AALuis intends to develop an open User Interface Layer that facilitates a dynamically adapted, personalized interaction between an elderly user and any kind of service, with different types of input and output devices and modalities. To achieve this the AALuis User Interface Layer keeps track of changes of a variety of information models to adapt the transformation process from abstract task descriptions to a user interface and to steer the user interaction in a suitable manner. One of the main goals of AALuis is to create and exploit synergies by developing an architecture that allows the easy integration into different established AAL middleware platforms. AALuis aims to significantly contribute to the freedom of choice for end-users of services and users interfaces.

A system is presented to display text information by an animated talking avatar suitable for health care services [5]. Speech animation parameters are calculated by a co-articulation model from the phone chain extracted from the text-to-speech processing step. An animation script that layers body movements and speech animation is generated and then rendered and converted into an h.264 video by a computer game engine. The animation system is attached to AALuis, an OSGi-based system for care services for older adults within a European research project.

Smartphone applications (Apps) provide a new way to deliver healthcare, illustrated by the fact that healthcare Apps are estimated to make up over 30% of new Apps currently being developed; with this number seemingly set to increase as the benefits become more apparent. In [6], using the development of an In Vitro Fertilisation (IVF) treatment stress study App as the exemplar, the alternatives of Native App and Web App design and implementation are considered across several factors that include: user interface, ease of development, capabilities, performance, cost, and potential problems. Development for iOS and Android platforms and a Web App using JavaScript and HTML5 are discussed.

In [7], a user-centered framework for redesigning health care interfaces was proposed. Numerous health care systems are designed without consideration of user-centered design guidelines. Consequently, systems are created ad hoc, users are dissatisfied and often systems are abandoned. This is not only a waste of human resources, but economic resources as well. In order to salvage such systems, the authors have combined different methods from the area of computer science, cognitive science, psychology, and human–computer interaction to formulate a framework for guiding the redesign process. The paper provides a review of the different methods involved in this process and presents a life cycle of our redesign approach. Following the description of the methods, the authors present a case study, which shows a successfully applied example of the use of this framework. A comparison between the original and redesigned interfaces showed improvements in system usefulness, information quality, and interface quality.

Regarding the assessment tools for healthcare interface, a pilot study is reported to identify an improved method of evaluating digital user interfaces in health care [1]. Experience and developments from the aviation industry and the NASA-TLX mental workload assessment tools are applied in conjunction with Nielsen heuristics for evaluating an Electronic Health Record System in an Irish hospital. The NASA-TLX performs subjective workload assessments on operators working with various human-computer systems. Results suggest that depending on the cognitive workload and the working context of users, the usability will differ for the same digital interface.

In the Eindhoven area, there have been quite some developments in the area of user interface for healthcare and wellbeing. For example,

1. Within the collaboration of TU/e and Máxima Medical Centre (MMC), a smart Jacket was proposed and designed as the vision of a wearable unobtrusive continuous monitoring system realized by body sensor networks (BSN) and wireless communication. The smart jacket has a shape of the natural interface for neonate (i.e. a baby jacket) and aims for providing reliable health monitoring as well as a comfortable environment for neonatal care and parent-child interaction. An iterative design process in close contact with the users and experts lead to a balanced integration of technology, user focus and aesthetics (Figure 7.7).

Figure 7.7: Smart jacket [8]

2. In collaboration with MMC, at TU/e ID, a design of wireless power supply was proposed based on the principle of inductive contactless energy transfer for use in Neonatal Intensive Care Units (NICU). The user interface was designed in a way that

the technologies were hidden in the background and the possibilities for aesthetic features were incorporated to fit the baby care setting. The proposed power supply satisfies the requirements of neonatal monitoring and provides continuous power when the neonate is inside the incubator or during Kangaroo mother care (Figure 7.8).

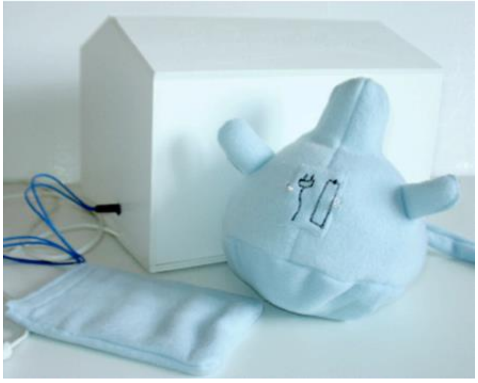

Figure 7.8: Power boy [9]

3. In collaboration of MMC, at TU/e ID an integrated sensor system—the "Rhythm of Life Aid" (ROLA) was proposed to support medical staff during cardiopulmonary resuscitation (CPR) of newborn infants. The design concept is based on interactive audio and visual feedback interface with consideration of functionalities and user friendliness. A prototype ROLA device is built, consisting of a transparent foil integrated with pressure sensor and electroluminescent foil actuators for indication of the exerted chest compression pressure, as well as an audio box to generate distinctive sounds as audio guidance for insufflations and compressions. To evaluate the performance of the ROLA device, a sensory mannequin and a dedicated software interface are implemented to give immediate feedback and record data for further processing (Figure 7.9).

Figure 7.9: Visual feedback of the ROLA prototype integrated with the FSR sensor and EL-foil actuator testing on a mannequin [10]]

4. Within the collaboration with Holst Centre IMEC NL and TU/e ID, a design of a feedback system for body worn wireless sensors was proposed to be used in wireless emotion monitoring. The user interface was designed to fit the working environment. The design aims to facilitate a working environment, which can take care of the wellbeing of employees to stay healthy, enjoy work and be able to develop. A prototype, the Smart Photo Frame has been made as the feedback device. This device provides employees feedback on the emotional arousal status in real-time, in an effort towards reducing work-related stressful states through

positive calming. The user interface is designed to be subtle in an office related environment (Figure 7.10).

Figure 7.10: Wireless emotion monitoring BAN and smart photo frame user interface [11]

7.3 User acceptance

The advance of technology is hard to predict, and the reaction of humans from society down to single users on this advanced technology is an even harder challenge. In this sense, we will try to summarize important trends in this section that will have a big impact on how people will deal with data and its representation through interfaces in the future. User acceptance of healthcare will be sketched below together with wellness related user interfaces in the following dimensions:

7.3.1 User Diversity

An important observation is that data and information in various forms enter our everyday life more and more, and this is a well-accepted reality for most people - especially from younger generations. Older generations and elderly are certainly not as fast as teenagers to adapt new paradigms of interaction, socially connecting and sharing, but they copy and learn as a need to blend into an ever-younger world with an overall youthful lifestyle and a wide consensus regarding the need to stay "young".

This is good news for the adoption and acceptance of data generated and mediated through technology and user interfaces as more and more people understand at least on a surface level how this data connects to their life, what the numbers on the display mean and what commonplace interpretations apply. This acceptance level is however, highly depending on the way data is presented and the conceptual gap between data generation or *production* and its presentation to *consumers*. Although it is expected that the tolerance for increasingly large gaps is developing over time, this is a gradual process of pushing comfort zones and reaching incrementally more sophistical levels of understanding of data and its relationship to reality.

End-users, the users who wear sensors, are presented with a first-hand account of the collected data, given to them in a tailored way. There is a spectrum of user archetypes in the context of wellness and healthcare related data generation and consumption: from the "quantified self" movement, via early-adopters and the digital native mainstream to elderly users. The first group can be seen as very eager to embrace and accept new methods to find out more about their health, however, they will also require extensive means to tinker with the data generation and data processing as well as being very conscious about data ownership and privacy. While early adopters, digital natives as a mainstream culture are expected to readily accept most new applications (if they make sense to them and their peer group), the *ever-younger ageing society* can be seen as a challenge of form giving as well as clever branding for data collecting devices: elderly who have a relatively young self-image require more and more devices that are same or similar to equipment used by younger adults and teenagers. This however needs to be achieved with taking the gradually lesser sensory and cognitive capabilities into account.

Professional users or professional/business stakeholders of user data will certainly have a more professional and less emotional attitude towards data collection and information processing. They will accept new user interfaces if the new design fits their workflow to some degree and have added information value to their monitoring, diagnostics and treatments. Compared to consumers, professional stakeholders will be considerably more tolerant towards tools that enable better healthcare and improve wellness.

As they will be likely the “observers” of behaviour and health status they will and must be in a different role and power position than the end-users of sensor-equipped devices: while professionals might even push end-users towards as full as possible coverage of daily life sensor data, they need to understand that they are operating from a more distant and less involved position, and need to seriously consider privacy issues, but also potential accessibility problems and difficulties in grasping the breadth of impact that gathering sensor data can have on everyday life. Therefore, any access to data gathering mechanisms and the data itself should be protected and mediated.

Apart from healthcare professionals and wellness applications, there will be organizations interested in getting access to users’ data and eager to push forward policies for data gathering and sharing. One example would be insurance companies that offer differently priced policies in exchange for collected data. But this might not evolve towards a voluntary offering, but instead towards a requirement which then has serious privacy implications.

Multiple users or the (extended) social network of patients will be another challenge for user interfaces in the health and wellness context, reaching from “giving the patient’s family access” to truly providing parallel interfaces to collected data. While this is interesting mostly for data consumption, data generation will be partly inspired and consists of group activities in the future. Games and competitive play are a good example for this: multiple people collect metrics about their performance or health status, and this information is fed into the game system that is collaboratively accessed by all players. This setting offers many means to boost behavioural change and awareness, often driven by competitive thinking, but it should be noted that the involvement of others in the personal health domain has privacy issues and can lead to mental stress and anxiety – naturally a detractor of user acceptance.

7.3.2 Accuracy and Measurability

In terms of accuracy and measurability, two important aspects add to user acceptance: (1) the nature of experienced “reality” by future users of products will be more dominated by systems and networked intelligence, and (2) user expect and require more and more aspects of reality measured, quantized, and made readily available for comparison, competition and self-improvement. Trusting in measurements and the accuracy thereof will contribute to user acceptance. A central question is also how accurate information needs to be, and whether raw numbers will actually benefit and afford user awareness leading potentially to behavioural change. In this context, accuracy diverges from the notion of precision towards conceptual and semantic accuracy to be meaningful to users. The granularity of data and the scales used to present it to users are key, and the normative component (what is high, low or average) becomes increasingly important, especially in the health domain.

Another question is about indirect measurements, and more in general, about measurability: what can be measured accurately to draw conclusions from, and what is only deducible from other (related) measurements. An example is given in [15] in which mobile phone position and communication patterns are related to physiologic and mental health of users. Other examples in the health domain are the Omnibus Risk Estimator[16] and the WHO FRAX [17] calculator, which are tools to estimate certain health risks (chances of suffering from *atherosclerotic cardiovascular disease* and *major osteoporotic fracture* respectively). While such number-based risk estimation tools can be highly helpful to medical decision-making, they are also highly controversial due to their aggressive abstraction from reality based on a few semi-reliable measures[18]. Independent from whether this is about devices, processes, services or algorithms, all of these technological interventions have an impact on the user acceptance in the sense that deductions and derivative data needs to be plausible (and the derivation mechanism transparent), but still close enough to the problem at hand to be accepted by users. There are huge opportunities in opening this range of tools to end-users by allowing them to measure and calculate themselves – and making use of healthcare professionals as interpretation and solution support based on hey have found out by themselves about their health condition.

7.3.3 Privacy and Big Data

Big data in the healthcare context has become a hot topic with an estimated 300 billion market potential [19], numerous European research projects and a general public awareness of the potential of using data in the context of healthcare and wellness make a strong case. By using aggregated datasets of millions of patients, pharmaceutical companies, insurance companies, and other major players in the health sector promise breakthroughs in terms of better diagnosis and care giving.

However, in the following, a more personal viewpoint on privacy shall be taken. The introduction of data into a traditionally very much person-to-person setting is a challenge: The biggest challenge in working with personal data (health data is *very* personal and rich compared to, e.g., social network data) is preserving actual and perceived privacy. Scientists cite scenarios, in which a patient's personal healthcare is made public – and then used by employers or insurance companies to the patient's disadvantage. On the other hand, health has been traditionally an area too complex to understand intuitively, but only through the expertise of a healthcare professional – at least for non-trivial diagnoses.

In principle, there are two important aspects to user-centered privacy: (1) should someone else know about some aspect of a person's health, and (2) if they should be allowed to know, do they know the correct information about the health aspect? The first question relates to user trust, accessibility, (inter-)national policy, business and legal matter, and more abstractly to the growing imbalance between users as the true providers of data and other parties benefitting from this without many obligations to compensate, protect and restrict the flow of data. Information can be compared to natural resources such as water, oil or soil, which when overused and exploited, will become scarce. Users are developing a better sense of data these days with more understanding and a better developed moral framework to make decisions about who should access their personal data in which way at what time for how long.

Looking at how health data is currently collected, used and accessed, there are over 40.000 health-related apps available on the app stores for iOS, Android and other platforms. Many of them rely on self-tracking by means of self-reporting, or using rudimentary sensors such as built-in acceleration sensors of modern smart phones. Few access electronic health records and other documentation about one's health. Finally, there are applications that use custom sensors to better track person body metrics such as breathing patterns, heart rate, sleep patterns, and skin conductivity. What relates these applications to Big Data is the scale on which people are measured and on which the data is fused into a large-scale database of human health conditions. It is yet unclear how well this data can be leveraged to actually improve health on a larger scale, apart from presenting simple body metrics to users. Often contextual information is not captured in the right modality, amount or accuracy to be useful or provide the correct context to the sensor data. This as well might have negative impacts on a user's reputation.

The second aspect directly relates to data generators, data storage and processing, semantic connections between data items, and general reliability: if a health metric is tracked over time and then interpreted algorithmically, is this interpretation a correct abstraction or model of the measured reality and should this model taken as a based for important health-related decisions? Also here, users have to have trust in how their data is handled and used for decision making, so it might become important to transparently communicate how data is processed, modeled and then leveraged in organization that have access to this data. While this can be seen as a big effort with enormous costs, it will build a better understanding that modern healthcare and wellness applications *need* good data and users will be more open and willing to provide data to initiatives with clear policies and good communication about data handling and their motivations.

7.3.4 Connectivity and Real-Time Data

Connectivity in the home or work place, but also in the urban environment will rather increase than decrease in the future. Devices that employ sensors will likely be able to directly share and stream this data with other devices, personal information storages and remote services in the cloud. While connectivity is an important precondition, the available bandwidth is a second requirement that will enable truly interesting applications based on data collected by small sensors in or on the human body and its proximity. Similar to expected developments on connectivity sufficient bandwidth for sensor data applications will likely be more available in the future. A third aspect is the connection speed that can range from very fast "pings", i.e., fast round trips between device and communication counterpart, to more lag in the communication, which is essential for real-time application of sensor data.

The need for real-time reactions to events raised based on the (local or remote) processing of sensor data depends largely on the type of application these events will rely on. As an example, there is a range from life-critical applications ("stroke pattern detected, consult expert advice immediately") to more casual life-logging applications ("you have run for 23mins and burned 340kcal, have an ice-cream now"). Real-time data as gathered from sensors in an appropriate format, quality and quantity will be available and therefore lead to even better input for more advanced signal processing algorithms. An important question will be how different industrial and academic efforts will attempt the commoditization of such a real-time sensor data infrastructure.

Finally, again the notion of relevance and meaning is important when thinking about timeliness of data: not only the spatial context and mindset matter, also that data arrives in a moment in which it is still relevant and useful. Data should relate to something the user cares about presently to take action or change behaviour.

7.4 References

[1] http://www.google.com/glass/start/
[2] https://www.leapmotion.com
[3] L. Longo, and B. Kane, "A novel methodology for evaluating user interfaces in health care", 24th International Symposium on Computer-Based Medical Systems (CBMS), 2011, pp. 1-6.
[4] Christopher Mayer, Martin Morandell, Matthias Gira, Kai Hackbarth, Martin Petzold, Sascha Fagel, "AALuis, a User Interface Layer That Brings Device Independence to Users of AAL Systems", Computers Helping People with Special Needs, Lecture Notes in Computer Science Volume 7382, 2012, pp. 650-657.
[5] Sascha Fagel, Andreas Hilbert, Christopher Mayer, Martin Morandell, Matthias Gira, Martin Petzold, "Avatar User Interfaces in an OSGi-based System for Health Care Services", The 12th International Conference on Auditory-Visual Speech Processing, 2013.
[6] Kirusnapillai Selvarajah, Michael P. Craven, Adam Massey, John Crowe, Kavita Vedhara, Nicholas Raine-Fenning, "Native Apps versus Web Apps: Which Is Best for Healthcare Applications?", Human-Computer Interaction. Applications and Services, Lecture Notes in Computer Science Volume 8005, 2013, pp. 189-196.
[7] Constance M. Johnson, Todd R. Johnson, Jiajie Zhang, "A user-centered framework for redesigning health care interfaces", of Biomedical Informatics 38 (2005) 75–87.
[8] Sibrecht Bouwstra, Wei Chen, Loe Feijs, Sidarto Bambang Oetomo, "Smart jacket design for neonatal monitoring with wearable sensors", in Proceedings of Body Sensor Networks (BSN), 2009, Berkeley, USA, pp. 162 - 167.
[9] W. Chen, C. L. W. Sonntag, F. Boesten, S. Bambang Oetomo, L. M. G. Feijs, "A Design of Power Supply for Neonatal Monitoring with Wearable Sensors", Journal of Ambient Intelligence and Smart Environments-Special Issue on Wearable Sensors, vol.1, no. 2, pp. 185 – 196, 2009, IOS press.
[10] W. Chen, S. Bambang Oetomo, L. M. G. Feijs, P. Andriessen, F. Kimman, M. Geraets, and M. Thielen, "Rhythm of Life Aid (ROLA) – An Integrated Sensor System for Supporting Medical Staff during Cardiopulmonary Resuscitation (CPR) of Newborn Infants", IEEE Transactions on Information Technology in BioMedicine, vol. 14, no. 6, pp. 1468-1474, Nov. 2010.
[11] Kimmy Ansems, Wei Chen, Lindsay Brown, "Smart Photo Frame for Arousal Feedback - Wearable sensors and intelligent healthy work environment", in proceedings of workshop on Smart Offices and Other Workplaces of the 7th International Conference on Intelligent Environments - IE'11, Nottingham, United Kingdom, July 2011, pp. 685-696.
[12] Daniel Sonntag, Ralf Engel, Gerd Herzog, Alexander Pfalzgraf, Norbert Pfleger, Massimo Romanelli, Norbert Reithinger, "SmartWeb Handheld — Multimodal Interaction with Ontological Knowledge Bases and Semantic Web Services", In: Artifical Intelligence for Human Computing LNCS 4451, 2007, pp. 272-29.
[13] Eric Morasch, "Weight Loss Diet Simulator Calorie Calculator BMI BMR Tool Counter", 2013, https://itunes.apple.com/us/app/id451491278
[14] Blum, T.; Kleeberger, V.; Bichlmeier, C.; Navab, N., "mirracle: An augmented reality magic mirror system for anatomy education," Virtual Reality Short Papers and Posters (VRW), 2012 IEEE, pp.115,116, 4-8 March 2012.
[15] Anmol Madan, Manuel Cebrian, David Lazer, and Alex Pentland. 2010. Social sensing for epidemiological behavior change. In Proceedings of the 12th ACM international conference on Ubiquitous computing (Ubicomp '10). ACM, New York, NY, USA, 291-300.
[16] http://www.cardiosource.org/en/Science-And-Quality/Practice-Guidelines-and-Quality-Standards/2013-Prevention-Guideline-Tools.aspx
[17] http://www.shef.ac.uk/FRAX/
[18] http://www.nytimes.com/2013/11/30/opinion/statins-by-numbers.html
[19] Peter Groves, Basel Kayyali, David Knott, and Steve Van Kuiken. 2013. The 'big data' revolution in healthcare: Accelerating value and innovation. Technical Report, McKinsey&Company. January 2013.

Chapter 8 Executive Summary & Recommendations

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With contribution of all working group members

8.1 Smart systems for Healthcare and Wellness

It is now recognized that the monitoring and prevention of diseases and follow-up of patients are two key components for improving the *quality of life*. The improvement in quality of life and the reduction of hospitalization bring associated cost savings at both the individual and societal levels. On the other hand similar technologies can be used for as personal trainers for wellbeing of active people. Smart systems for health and wellbeing are specially designed to simultaneously measure many physical and physiological parameters. Captured data can be analysed in real time to provide the physiological status of the person wearing the device. Such body parameters are useful for recording the physiological status of healthy people as well as that of people with a chronic disease or frailty.

In smart systems dedicated to healthcare and wellness applications the sensors collect physical, chemical and biochemical data to enable interpretation and monitoring of a person's physiological status, in relation to the actual environmental and social context. To afford a complex multi-parametric real-time sensing based on several types of sensors in portable smart systems, the power consumption per sensor element becomes a figure of merit as important as the other requirements (sensitivity, selectivity, robustness, reliability, integration on advanced silicon platform and/or flexible substrates). The power figure should include the power required by readout electronics, signal conditioning and AD conversion, but usually exclude digital signal processing such as linearization, pattern recognition and sensor fusion.

Covering all the available technologies within one report is impossible. Therefore we have restricted ourselves to a specific subset. The characteristics are

- The devices are to monitor specific body signals, intermittently or continuously and linked to an individual. Therefore they are on or near the body, embedded in clothing or implanted for a certain period of time.
- They should be comfortable and unobtrusive. This set upper limits to their dimensions and weight. Typically they are in the order of mm to cm's. This is especially important for implanted devices
- The devices either store their data internally and are read out regularly, or they are wirelessly linked to a central hub (e.g. cell phone), which enables to share the data externally.
- The devices should be autonomous, which means that there should be sufficient energy available to operate the device during the required lifetime of the application. This can range anywhere from a few minutes to a few months.

8.2 Applications Cases

Application cases for smart systems can be broadly divided between systems designed and marketed for clinical scenarios and applications, and those targeting the consumer market, addressing more general health and wellbeing markets. The associated regulatory stringency requirements ranges from systems required for enabling clinical decision support, to devices and systems intended for the consumer market to promote wellness through informed lifestyle choices. In this report a subdivision between the health and wellness applications is made as follows:

Clinical applications related to:

(a) **Pregnancy and neonatal monitoring**: The primary aim is to enable early indication of any adverse changes in the health status of either mother or foetus
(b) **Critical care monitoring:** providing each patient on admission to hospital with some form of minimally invasive, wireless and wearable system which tracks a range of physiological parameters, movement through the hospital, and progress during recovery and for an initial period following discharge.
(c) **Clinical competency assessment:** Smart systems provide a new opportunity to address the challenges of new regulatory requirements to monitor the performance of clinicians during each of the microtasks involved in performing a procedure. Such monitoring provides a basis for objective analysis of clinical performance
(d) **Post procedure rehabilitation and monitoring:** Systems will collect physical data, in order to assess and store the state of health of the patients, the exercise and therapy plans, and the therapy progress. Secure transmission of data needs to be assured and the system needs to be easily connected to a rehabilitation centre.

And wellness applications:

(e) **Informed health and wellbeing including healthy and active ageing:** Preventing people becoming sick. Examples are the measurement of stress and the assistance in fitness training
(f) **Personal safety:** the development of miniaturized pollution monitoring solutions that can be integrated in wearables. Such devices ultimately can be integrated into a big network, sharing all data.
(g) **Enabling independent living for persons with intellectual / cognitive disabilities:** While modern healthcare enables people to live significantly longer, their physical and intellectual condition in the latter years, can compromise the ability to live independently without additional supports. Similarly, there is a clear consensus and regulatory requirement that people with intellectual disabilities should be facilitated to live in the community rather than reside within institutional care.

There are many examples of current devices which function well technically, but are not acceptable to or suitable for the end user due to complexity, size, perceptions of social stigma, etc. Therefore, a detailed engagement with end users is required to understand the priorities of the design team, where compromises may be required. Essential requirements include low cost, disposable modules to facilitate hygiene, scale/ergonomics compatible with the use case scenarios and related social considerations, avoidance of any installation or maintenance needs, and the ability to engage the end user in a positive way for using the device and/or system

8.3 Sensors and Actuators

Selected topics from the wearable and implantable smart systems scenarios were discussed in the report, with a main focus on the first ones, which encompass solutions with a reduced degree of invasiveness. However, as the frontier between an invasive and non-invasive smart system is frequently difficult to precisely define, some relevant emerging sensors for implantable smart systems have been included, especially where the respective research is advanced in Europe and/or the potential economic and/or societal impact is large:

- **Wearable Electro-physiological sensors (EXG) and electrodes**

Hardware, electronics and algorithms still need optimization towards optimal performance of dry electrodes in combination with high user comfort and easy device handling. Motion artifact reduction, miniaturization of the electrode and introducing mechanical flexibility is important. Ohmic dry electrodes can be used in a passive way for ECG, but for smaller biopotentials an active electrode is essential. For capacitive electrodes, active electrodes are always required. Integration of the electrodes into a comfortable elastic band, cap or headset still needs attention. Also the pressure of the electrode on the skin should be realized such that skin irritation or pain is avoided.

Regarding the systems electronics ultra-low-power electronics are essential to avoid bulky batteries, which is in contrast to the higher demands on signal quality and multifunction-sensor systems.

In order to obtain a low-cost unobtrusive and widely acceptable devices a few problems need to be solved. First, it's clear that the body (chest) surface is only locally flat, a conformable/flexible or stretchable system will allow direct epidermal electrical measurement. Sensing interface has to be minimally invasive, conformable to human body and easy to wear, the recent developments of new sensing cloths that allow the recording of physiological signals demonstrate the potential of such approach. The innovation in term of textile is related to the use of functional yarns integrated in the fabric for sensing and acquisition of vital signs. In this kind of design, electrodes and connections are all integrated in the textile material, the remaining electronics board use traditional technology.

- **Implantable Electro-physiological sensors (EXG) and electrodes**

In the clinical practice, the tendency is toward systems having high number of electrode channels that each provides localized stimulation and recording. The strict anatomical constraints require achieving smaller and thinner medical devices. To reach these goals, the development of technology with multiple metal levels to make denser routing is necessary.

The evolution of Multi Electrode Array (MEA) has arrived at a level where packaging restricts the achievable performance of the final device. The packaging of the electrodes with high number of active area requires elaborating a reliable collective and flexible solution. As the pitch size decreases, reliable fabrication of interconnections is more challenging.

The size of multiple wirings is a limiting factor to increase the number of electrodes. Novel solutions have to be contemplated: multiplexing, optical control with asynchronous camera, hybrid interface. The signal processing is a key component when the number of sensors or active area increases drastically.

Electrode properties often changes over time, the exact factors need to be identified. The closed loop of the medical system will have to include the measurement of the quality control of the electrodes. Recently, the performance and stability of microelectrodes is improved by the use of biologically inspired electrode treatment. The promising enhancements of the flexible electronics offer tremendous opportunities for the neural prostheses: especially for the signal conditioning. The development of the association of the MEA with flexible electronics is one of the key to extend the functionality, and also to mitigate inflammatory and encapsulation processes in the surrounding tissue.

For the leadless pacemaker and more generally for the neural prostheses, the development of ultra-miniature electronics have to include: high density submicron technology chips, the RF transmission, low leakage high density battery, etc. The size of the battery is a limiting factor for miniaturization of medical device.

- **MEMS sensors for human physical activity: accelerometers and gyroscopes**

The SOI CMOS technology allows the integration of *Nano-Electro-Mechanical-Systems (NEMS)* accelerometers in the front-end, therefore combining the CMOS circuitry and the NEMS devices in an even more compact way. However, the use of NEMS raises important problems to the capacitive detection schemes and their integration because an extremely small variation of a capacitance has to be detected with low power consumption and reasonable SNR. The full compatibility with SOI CMOS front-end ensures the integration of the sensor and circuitry with reduced parasitic and enables the use of thin film packaging techniques at wafer level.

- **Bio-chemical sensors**

Standard dielectric materials normally employed in microelectronics technology can be used in making ion-sensitive field-effect transistors and ion-selective microelectrodes for bio-sensing applications. The future challenge is to properly integrate all the components (polymer membrane, biochemical compound and micro-electrodes) of the biosensor coupled with the electronics circuits in a robust and practical manner and to validate in real conditions the functions.

- **Sensors for gas and airborne particles**

For wearable sensors, outdoor sensors and sensors in buildings, zero-power technology is essential. Battery-based consumer devices lack communication functionality and run into problems with empty batteries. Also, the reduction of installation cost is essential, and the devices need to be self-sustaining over long periods of.

Most of the gas sensing technologies listed have the potential to reach the targeted power consumption figures. Open challenges for these technologies are related to their lack of selectivity and insufficient characterization with respect to environmental parameter variations. Large scale fabrication technologies with acceptable yields are also waiting to be developed. The situation for sensors for particle and airborne pathogens is much more unclear. This field is virtually in its infancy with no commercial products available yet and only a few academic demonstrations.

- **Integration on patches**

The future patch must be light weight, take the shape of the object on which it is fixed, and follow all complex movements of the host (possibly taking advantage of those movements to harvest energy to the device): explaining the need for elasticity. A typical patch will have several functionalities to collect, transport, analyse samples, deliver drugs and communicate with the outside (smart phone).

- **Micro-pumps and actuators**

Personalized medicine is going to become increasingly importance. Drug delivery micro-pumps will follow. Physical, physiological sensors (EXG, blood pressure) and biological sensors, integrated directly into micro-pumps, or part of the global delivery system, will be able to control the therapeutic effect. Apart from the technology issues, regulatory aspects such as biocompatibility, toxicity, clinical trials or CE marking and safety and security should be taken into account from the beginning,

Actuators will benefit of the development of soft devices, and could be integrated into patches. For example, vibration of piezoelectric materials could be exploited for micro-massages. Localized heating is also a possible interesting application. Electronics could be based on organic electronics. Negative wound pressure therapy is a recently introduced treatment. In the field of glasses or eye-lenses, improvements should benefit of the recent development of auto-adaptive lenses for optics.

8.4 Sensor Electronics & Signal Processing

Healthcare and wellness applications require variety of signals including bio-signals, bio-markers, environment variables, etc. In spite of a vast amount of different sensors, all the processed signals are related to physiological signals, biologic parameters or environmental, so they are generally low frequency, and low amplitude signals. Recent studies have even proved that a 20Hz sampling frequency and 12 bits resolution were enough for analysing human movements.

Some of the Sensor Electronics issues discussed are

- **Sensor front-end architecture**

Low noise instrumentation: The main specifications for an Instrumentation Amplifier (IA) are its accuracy (or noise), and power dissipation: for a low power budget, a trade-off has to be made between them. In many bio signal applications, multi-channel monitoring was proved necessary to achieve better physiology comprehension and event detection. The major drawbacks in these multi-channel chips are the increase in area and power consumption, and the risk of crosstalk between channels.

Analog-to-digital conversion: To optimize power and area budget, multiplexed architectures are used to mutualize processing resource. Since bio-signal are low bandwidth, the analog-to-digital converter can be shared between different channels. In the field of healthcare applications, the Successive-Approximation-Register ADC is a good candidate. For medium-frequency applications (few kHz), it actually presents a good compromise between power and resolution.

Co-integration: Besides the classical direct measurements approach, more and more works describe co-integrated architectures. Last evolution in healthcare sensors is the development of electrochemical sensors, where the potentiometric approach is preferred: a device is fabricated with a gate electrode which is sensitive to the detected substance. In ion-selected field-effect transistor (ISFET), drain-source current is proportional to pH, whereas is ENFET, drain-source current is proportional to an enzyme concentration. Main drawback of these sensors is that they are not compatible with CMOS processes.

- **Adaptive sensor readout circuits**

Next generation of readout circuit will have to comply with an increasing number of sensor outputs. Increasing the number of readout circuits on a same die will put harsh constraints on both silicon area and power consumption of readout circuits. Great power savings are to be expected from systems fully aware of their environment and which can adapt their behaviour subsequently.

- **Integrated Control and Signal Processing**

A sensor/actuator node requires embedded processing to handle control, signal processing as well as protocols. The systems discussed will be energy constrained with various operating duty cycles. The following emerging techniques are very promising: **Near/Sub-threshold computing, Co-processing and specialized co-processors, Adaptive and imprecise architectures**

- **Assisted Signal Processing and Compressed Sensing**

Efficient task partitioning between the analog and digital domains is a vital consideration for the system power reduction given the fact that majority of the biopotential acquisitions systems are mixed signal in nature. It is possible to reduce the system power consumption by carefully offloading the tasks that require limited SNR to analog domain and perform rest of the tasks in digital domain. The other application domain where the assisted signal processing is gaining attention is in feature extraction and classification. Compressed sensing is a novel signal acquisition method which can be used to recover sparse signals by sampling at rates far below the conventional Nyquist rate. This can lead to significant power savings in the analog to digital conversion and transmission

- **Emerging Integrated Systems**

Implantable Systems: Neural implant applications can be classified in three categories: sensory prosthetics, brain pacemakers and brain computer interfaces (BCIs). The current trend in neural interfaces is to achieve massive parallel recording while minimizing power and area consumptions. This requires the development of low-power circuit techniques, efficient data management and smart power scheduling

Wearable Systems: The emerging wearable EEG systems must facilitate the high-quality EEG recording in a non-invasive and comfortable manner. For ECG, complete cardiac readout ICs have been developed to meet the increasing interest for unobtrusive, ultra-low power, long-term cardiac monitoring devices recently.

On the topic of Signal processing, the following conclusions are made:

- Close-loop systems are becoming more and more ubiquitous: this bridges the gap between the biomedical signal processing domain with robotics and automatics. This will impact applications like actuators for drug delivery or Electrical stimulation and the control of insulin injection through the processing of glucose sensor data.
- The biomedical signal processing is more and more using biomedical modeling and simulation. This approach is heavily used in inverse problems (EEG/MEG source localization approaches or EIT reconstruction algorithms). Modeling also can be used to predict signal SNR for a given system geometry or under given system parameters.
- A more and more intimate link is now made between biomedical signal processing and statistics, multivariate data analysis or machine learning. Since data are becoming more and more complex, it is now mandatory to project it into meaningful subspace to carry out further processing. Bioinformatics is also heavily relying on multivariate data analysis to identify relevant proteins or molecules for a given disease. Inverse problems can be combined to this feature selection.

8.5 Integration and packaging

Packaging and integration technologies for electronics used for wearable or implantable applications are currently under development, addressing the specific needs of this application field.

Wearable devices often need conformity to the body, and need to be small and thin, in order to provide the necessary wearing comfort to ensure patient compliance. Hence flexible or even stretchable electronic systems are needed, such realizations require dedicated material and technology developments to ensure high quality component and system packages. To realize flexible electronics, extreme chip thinning is essential.

In case of direct skin contact of a wearable device, biocompatibility of the contacting materials is an issue. For electronic devices integrated into textile, washability is often an essential requirement, putting severe demand on the hermeticity of the device/component package. Package reliability of the wearable device is important: multiple bending or stretching cycles should not result in material cracks, delamination of embedding polymers, etc. All these requirements ask for further material development for flexible and stretchable wearable electronics, always depending on the particular device application:

thinner/smaller passive components, polymers enabling thinner embedding without losing reliability, biocompatible interconnect materials and/or polymers, materials with excellent diffusion barrier properties for improved hermeticity, etc. Finally, all material developments should be performed with cost aspects in mind.

For **implanted electronics**, packaging and integration technologies differ strongly from conventional practices for standard electronics. Biocompatibility and biostability are of utmost importance and are contextual properties, hence no 'one-method-fits-all' packaging solution exist. More development regarding materials and test protocols for various applications is essential. Furthermore, the package reliability needs to be very high, certainly for long term implants. The harsh fluidic environment of the functional device requires excellent hermeticity. The need for materials with are excellent bi-directional diffusion barriers is still high, as well as packaging technologies combining such barrier materials with biocompatible metallization schemes and polymer embedding. Noble metals as gold or platinum are interesting biomaterials but they are very expensive, hence the development of cost-effective biocompatible metallization schemes would be an important step forwards regarding cost-reduction of electronic implants. As described in chapter 5, standard bio-responses in the human body upon device implantation, such as the FBR or biofilm formation, can cause severe medical problems or device malfunctioning, both issues definitively need to be prevented. Hence more investigation is required regarding package surface modification or the use of additional functional coatings. Finally, lack of certain dedicated test protocols make the development of an implanted device far from easy.

8.6 Data storage & Communication

Data processing, storage and communication are essential functionalities of future smart systems; their use in healthcare and wellness applications requires a very high level of integration for these devices to be worn on, or implanted in the human body without impact on the activities they have to monitor and no discomfort for the patient/user.

Regarding antennas, issues to be tackled are miniaturization and integration (in the HF/UHF range, the size and form factor are limited to sub-wavelength dimensions), antena-transceiver codesign and tunability (to enable extreme antenna size reduction, better RF performances and lower power consumption), propagation around and through the body (incorporating the effect of human tissue) and EM exposure and dosimetry (to tackle the effect increasing number of sources).

These integration constraints as well as the very specific operational environment of healthcare and wellness applications trigger some challenges in terms of wireless communications between these smart systems, whether they operate in networks or as stand-alone systems. First of all communication protocols able to guarantee both a high level of robustness and energy efficiency, but also security and privacy are needed. The wireless communication systems shall also support radio-localization functions (e.g. UWB), which will enable a wealth of novel applications. The standardization activity in this area is very important to ensure the level of performance and interoperability expected from these systems. Main Actors here are IEEE, Zigbee Alliance and the Continua Health Alliance.

Low power RFIC design and architectures on advanced silicon technologies become important. Other research elements to be tackled are polymer RF electronics, heterogeneous integration and integrated SoC design.

Processor systems need to support a wide range of bio-medical applications, but also several aspect of communication protocol handling. Topics in biomedical data processing are: Multi-core systems for energy efficiency, Dynamic performance scaling, and Dynamic frequency voltage scaling.

Data memory is mostly needed in biomedical applications to locally store sensor information or user data. Energy efficiency, cost efficiency, but also safety and security needs to get further evaluated to find out which type of memory and memory partitioning best serves the application level needs

8.7 User Interface & Acceptance

The technology that is currently emerging for high-tech gadgets, targeting early adopters such as Google Glass, Leap Motion UI and voice-based interfaces, will gradually reach maturity, enter the mainstream market and by doing so become "visible" to the rather conservative - regarding new user interface and novel interaction paradigms - domain of healthcare and wellness products.

With the technology available and sufficiently matured, miniaturized, integrated and adopted by R&D teams via open APIs and specification, new user interfaces will emerge effortlessly. It is nowadays well understood how to leverage the Internet and development communities to bring new technology fast to a global market starting with reference implementations, demonstrators, and SDKs, via early adopting academic users to the broader range of commercial use and finally commoditization. Several strong trends towards miniaturization, integration, reduction and simplicity, tangibility and ubiquity will continue in the coming years – even with increasing pace.

User acceptance, however, is a slower process. As it also depends on the content conveyed by such new interface, how the interface's form, function and interactivity can meaningfully contribute to the information and communication thereof. While technology push is generally strong and fast paced in many areas, the domain of health and wellness-related applications tends to be a slightly more conservative domain with more consideration and restraints towards adopting new technology – which should be regarded as a positive trait: it allows to consciously make better decisions on what is really needed and beneficial for all stakeholders, how to control the inherent risks and manage reliability of new technology, and how to migrate safely between different stages of the technological evolution. Given the right understanding of what user interfaces and user acceptance mean in the domain of health and wellness, there is a great future for next-generation user interfaces and user interaction with healthcare and wellness related datasets.

As a conclusion, it becomes clear that technology is currently emerging from high-tech gadgets targeting early adopters such as Google Glass, Leap Motion UI and voice-based interfaces and will gradually reach maturity, enter the mainstream market and by doing so become "visible" to the rather conservative - regarding new user interface and novel interaction paradigms - domain of healthcare and wellness products.

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Smart Systems for Healthcare and Wellness